STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 202255

TO: Anish Gupta
Location: rem/3A59/3C18
Art Unit: 1654
Friday, September 22, 2006
Case Serial Number: 10/764288

From: Saloni Sharma
Location: Biotech-Chem Library
REM-1A64
Phone: (571)272-8601

saloni.sharma@uspto.gov

Search Notes

Examiner Gupta,

See attached results.

If you have any questions about this search feel free to contact me at any time.

Thank you for using STIC search services!

Saloni Sharma
Technical Information Specialist
STIC Biotech/Chem Library
(571)272-8601

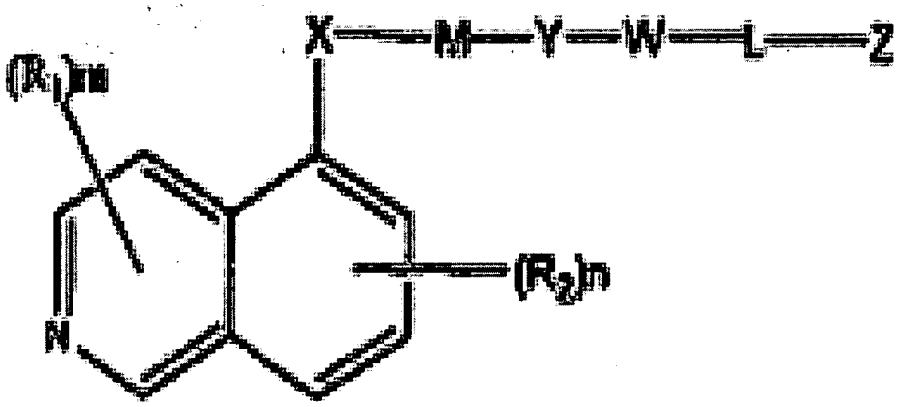
STIC-Biotech/ChemLib 9-966 202255 MG

From: Gupta, Anish
Sent: Tuesday, September 19, 2006 5:05 PM
To: STIC-Biotech/ChemLib
Subject: RE: SEARCH REQUEST

Search Request:

Name: Anish Gupta
Examiner #: 73121
date: 7-12-06
Art Unit: 1654
Phone # 2-965
Serial Number 10/764288 Location: 3A59
Mailbox #: 3C18

Please search the following structure



Formula I

MG

Searcher: Sabrina Shere
Searcher Phone:
Date Searcher Picked up: 9/23/06
Date completed: 9/23/06
Searcher Prep Time: 120
Online Time: 60

Type of Search
NA# [redacted] AA#:
S/L: Oligomer:
Encode/Transl:
Structure #: Text:
Inventor: Litigation:

Vendors and cost where applicable
STN: ✓
DIALOG:
QUESTEL/ORBIT:
LEXIS/NEXIS:
SEQUENCE SYSTEM:
WWW/Internet:
Other (Specify):

STIC
Scientific & Technical Information Center

STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact ***the searcher or contact***:

Mary Hale, Information Branch Supervisor
571-272-2507 Remsen 1 A51

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* ☐ *Example: 1610*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
  (journal articles, conference proceedings, new product announcements etc.)

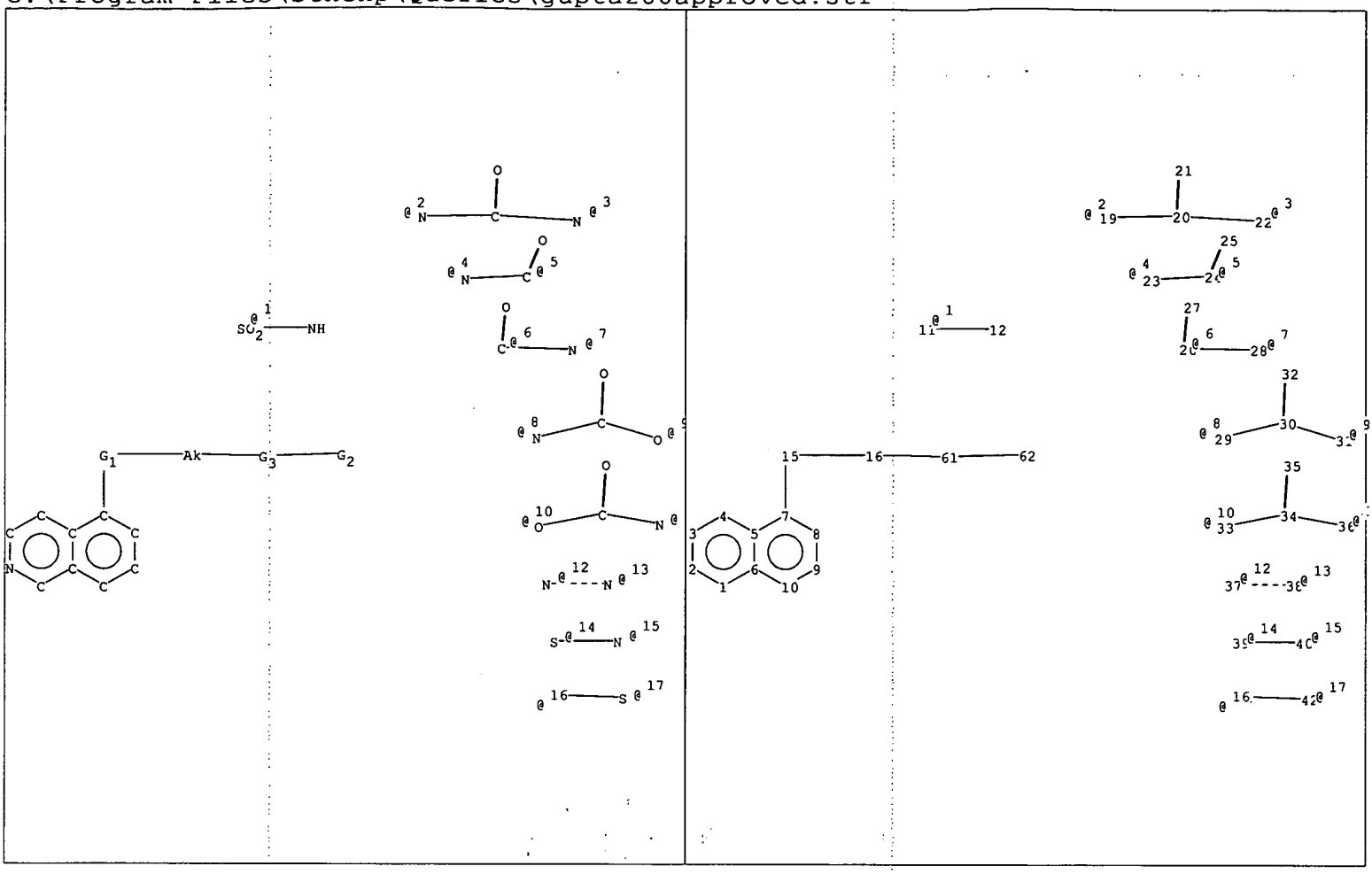
- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/Biotech-Chem Library, Remsen Bldg.

sira
Search and Information Resources Administration

C:\Program Files\Stnexp\Queries\gupta288approved.str



chain nodes :
11 12 15 16 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33
34 35 36 37 38 39 40 41 42 61 62
ring nodes :
1 2 3 4 5 6 7 8 9 10
chain bonds :
7-15 11-12 15-16 16-61 19-20 20-21 20-22 23-24 24-25 26-27 26-28
29-30 30-31 30-32 33-34 34-35 34-36 37-38 39-40 41-42 61-62
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10
exact/norm bonds :
7-15 11-12 15-16 16-61 19-20 20-21 20-22 23-24 24-25 26-27 26-28
29-30 30-31 30-32 33-34 34-35 34-36 37-38 39-40 41-42 61-62
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 8-9 9-10

G1:O,S,[*1]

G2:Cy,Ak

G3:N,[*2-*3],[*4-*5],[*6-*7],[*8-*9],[*10-*11],[*12-*13],[*14-*15],[*16-*17]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom
10:Atom 11:CLASS 12:CLASS 15:CLASS 16:CLASS 19:CLASS 20:CLASS
21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS
28:CLASS 29:CLASS 30:CLASS 31:CLASS 32:CLASS 33:CLASS 34:CLASS
35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 40:CLASS 41:CLASS
42:CLASS 61:CLASS 62:CLASS
Element Count :
Node 16: Limited
C,C1-4

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=> d his nofile

     (FILE 'HOME' ENTERED AT 13:24:41 ON 22 SEP 2006)

     FILE 'REGISTRY' ENTERED AT 13:24:45 ON 22 SEP 2006
L1                STRUCTURE UPLOADED
L2              8 SEA SSS SAM L1

     FILE 'CAPLUS' ENTERED AT 13:25:24 ON 22 SEP 2006
                  E US2004-764288/APPS
L3              1 SEA ABB=ON  PLU=ON  US2004-764288/AP
                  SEL RN L3

     FILE 'REGISTRY' ENTERED AT 13:26:32 ON 22 SEP 2006
L4             11 SEA ABB=ON  PLU=ON  (119-65-3/BI OR 148640-14-6/BI OR 494824-84
                  -9/BI OR 494824-85-0/BI OR 494824-86-1/BI OR 494824-87-2/BI OR
                  494824-88-3/BI OR 494824-89-4/BI OR 494824-90-7/BI OR 494824-91
                  -8/BI OR 56-65-5/BI)
L5              0 SEA ABB=ON  PLU=ON  L2 AND L4
L6              9 SEA ABB=ON  PLU=ON  L4 AND NC5-C6/ES
                  D SCAN
L7            225 SEA SSS FUL L1
                  SAVE L7 GUPTA288/A TEMP

     FILE 'STNGUIDE' ENTERED AT 13:31:46 ON 22 SEP 2006

     FILE 'REGISTRY' ENTERED AT 13:32:24 ON 22 SEP 2006
L8              4 SEA ABB=ON  PLU=ON  L7 AND L4
                  D SCAN
L9              4 SEA ABB=ON  PLU=ON  L7 AND SQL/FA
L10             4 SEA ABB=ON  PLU=ON  (L8 OR L9)
L11             7 SEA ABB=ON  PLU=ON  L4 NOT L8
                  D SCAN
L12             7 SEA ABB=ON  PLU=ON  L4 NOT L7
L13             4 SEA ABB=ON  PLU=ON  L12 AND SQL/FA
L14           229 SEA ABB=ON  PLU=ON  (L7 OR L13)

     FILE 'CAPLUS' ENTERED AT 13:35:37 ON 22 SEP 2006
L15           224 SEA ABB=ON  PLU=ON  L14

     FILE 'REGISTRY' ENTERED AT 13:35:47 ON 22 SEP 2006

     FILE 'STNGUIDE' ENTERED AT 13:36:26 ON 22 SEP 2006

     FILE 'REGISTRY' ENTERED AT 14:21:17 ON 22 SEP 2006
L16               STRUCTURE UPLOADED
L17             7 SEA SSS SAM L16
                  D QUE L1

     FILE 'REGISTRY' ENTERED AT 14:34:05 ON 22 SEP 2006
L18               STRUCTURE UPLOADED
L19             7 SEA SSS SAM L18

     FILE 'STNGUIDE' ENTERED AT 14:34:49 ON 22 SEP 2006

     FILE 'CAPLUS' ENTERED AT 14:35:33 ON 22 SEP 2006
L20           137 SEA ABB=ON  PLU=ON  L15 AND (PY<2001 OR AY<2001 OR PRY<2001)
L21           167 SEA ABB=ON  PLU=ON  L14 (L) (THU OR DMA OR PKT OR PAC OR
                  BAC)/RL
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L22          93 SEA ABB=ON  PLU=ON  L21 AND (PY<2001 OR AY<2001 OR PRY<2001)

     FILE 'STNGUIDE' ENTERED AT 14:37:18 ON 22 SEP 2006

     FILE 'REGISTRY' ENTERED AT 14:39:27 ON 22 SEP 2006
L23             STRUCTURE UPLOADED
L24           7 SEA SSS SAM L23
L25           7 SEA SUB=L7 SSS SAM L23
L26         206 SEA SUB=L7 SSS FUL L23

     FILE 'CAPLUS' ENTERED AT 14:40:26 ON 22 SEP 2006
L27         215 SEA ABB=ON  PLU=ON  L26
L28             ANALYZE PLU=ON  L27 1- RN :   16811 TERMS
                D

     FILE 'REGISTRY' ENTERED AT 14:40:59 ON 22 SEP 2006
L29           1 SEA ABB=ON  PLU=ON  147318-81-8
                D SCAN
L30           1 SEA ABB=ON  PLU=ON  144114-21-6
                D SCAN
L31           1 SEA ABB=ON  PLU=ON  155213-67-5
                D SCAN
L32           1 SEA ABB=ON  PLU=ON  127779-20-8
                D SCAN
L33           1 SEA ABB=ON  PLU=ON  150378-17-9
                D SCAN
L34           1 SEA ABB=ON  PLU=ON  30516-87-1
                D SCAN
L35           1 SEA ABB=ON  PLU=ON  161814-49-9
                D SCAN
L36           1 SEA ABB=ON  PLU=ON  159989-64-7
                D SCAN
L37           1 SEA ABB=ON  PLU=ON  69655-05-6
                D SCAN
L38           1 SEA ABB=ON  PLU=ON  7481-89-2
                D SCAN
L39         206 SEA ABB=ON  PLU=ON  L26 NOT (L31 OR L33 OR L34 OR L35 OR L37)
L40         225 SEA ABB=ON  PLU=ON  L7 NOT (L31 OR L33 OR L34 OR L35 OR L37)
L41           0 SEA ABB=ON  PLU=ON  L7 AND (L31 OR L33 OR L34 OR L35 OR L37)
L42           1 SEA ABB=ON  PLU=ON  L14 AND 147318-81-8
L43           0 SEA ABB=ON  PLU=ON  L14 AND 144114-21-6
L44           0 SEA ABB=ON  PLU=ON  L14 AND 155213-67-5
L45           0 SEA ABB=ON  PLU=ON  L14 AND 127779-20-8
L46           0 SEA ABB=ON  PLU=ON  L14 AND 150378-17-9
L47           0 SEA ABB=ON  PLU=ON  L14 AND 30516-87-1
L48           0 SEA ABB=ON  PLU=ON  L14 AND 161814-49-9
L49           0 SEA ABB=ON  PLU=ON  L14 AND 159989-64-7
L50           0 SEA ABB=ON  PLU=ON  L14 AND 69655-05-6
L51           0 SEA ABB=ON  PLU=ON  L14 AND 7481-89-2
L52         228 SEA ABB=ON  PLU=ON  L14 NOT 147318-81-8
L53           1 SEA ABB=ON  PLU=ON  L14 NOT L52

     FILE 'CAPLUS' ENTERED AT 14:49:13 ON 22 SEP 2006
L54          95 SEA ABB=ON  PLU=ON  L52
L55         129 SEA ABB=ON  PLU=ON  L15 NOT L54
L56         153 SEA ABB=ON  PLU=ON  L53
L57         129 SEA ABB=ON  PLU=ON  L56 NOT L54
L58          79 SEA ABB=ON  PLU=ON  L57 AND (PY<2001 OR AY<2001 OR PRY<2001)
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     FILE 'REGISTRY' ENTERED AT 14:50:44 ON 22 SEP 2006
L59         205 SEA ABB=ON  PLU=ON  L26 NOT 147318-81-8

     FILE 'CAPLUS' ENTERED AT 14:51:15 ON 22 SEP 2006
L60          86 SEA ABB=ON  PLU=ON  L59
L61         129 SEA ABB=ON  PLU=ON  L27 NOT L60
L62         129 SEA ABB=ON  PLU=ON  (L57 OR L61)
L63          79 SEA ABB=ON  PLU=ON  L62 AND (PY<2001 OR AY<2001 OR PRY<2001)
L64             ANALYZE PLU=ON  L15 1- RN :   19010 TERMS
                D
L65         153 SEA ABB=ON  PLU=ON  L29
L66         153 SEA ABB=ON  PLU=ON  (L56 OR L65)
L67         129 SEA ABB=ON  PLU=ON  L66 NOT L54
L68         129 SEA ABB=ON  PLU=ON  (L57 OR L67)
L69          79 SEA ABB=ON  PLU=ON  L68 AND (PY<2001 OR AY<2001 OR PRY<2001)
L70          79 SEA ABB=ON  PLU=ON  (L63 OR L69)

     FILE 'HCAPLUS' ENTERED AT 14:54:02 ON 22 SEP 2006
                E LIVNAH N/AU
L71          13 SEA ABB=ON  PLU=ON  ("LIVNAH N"/AU OR "LIVNAH NURIT"/AU)
                E YECHEZKEL T/AU
L72          16 SEA ABB=ON  PLU=ON  ("YECHEZKEL T"/AU OR "YECHEZKEL TAMAR"/AU)

                E SALITRA Y/AU
L73          11 SEA ABB=ON  PLU=ON  ("SALITRA Y"/AU OR "SALITRA YOSEF"/AU OR
                "SALITRA YOSEPH"/AU OR "SALITRA YOSPHE"/AU OR SALITRE/AU)
                E PERLMUTTER B/AU
L74           6 SEA ABB=ON  PLU=ON  ("PERLMUTTER B"/AU OR "PERLMUTTER B H"/AU
                OR "PERLMUTTER BORIS"/AU)
                E OHNE O/AU
L75           3 SEA ABB=ON  PLU=ON  ("OHNE O"/AU OR "OHNE ONSAT"/AU OR "OHNE
                OSNAT"/AU)
                E COHEN I/AU
L76         553 SEA ABB=ON  PLU=ON  ("COHEN I"/AU OR "COHEN I A"/AU OR "COHEN
                I BERNARD"/AU OR "COHEN I C"/AU OR "COHEN I E"/AU OR "COHEN I
                J"/AU OR "COHEN I K"/AU OR "COHEN I KELMAN"/AU OR "COHEN I
                L"/AU OR "COHEN I M"/AU OR "COHEN I R"/AU OR "COHEN I RANDELL"/
                AU OR "COHEN I ROY"/AU OR "COHEN I S"/AU OR "COHEN ILAN"/AU OR
                "COHEN ILANA"/AU)
                E LITMAN P/AU
L77          13 SEA ABB=ON  PLU=ON  "LITMAN PNINIT"/AU
                E SENDEROWITZ H/AU
L78          35 SEA ABB=ON  PLU=ON  "SENDEROWITZ HANOCH"/AU
L79           9 SEA ABB=ON  PLU=ON  (L71 AND (L72 OR L73 OR L74 OR L75 OR L76
                OR L77 OR L78)) OR (L72 AND (L73 OR L74 OR L75 OR L76 OR L77
                OR L78)) OR (L73 AND (L74 OR L75 OR L76 OR L77 OR L78)) OR
                (L74 AND (L75 OR L76 OR L77 OR L78)) OR (L75 AND (L76 OR L77
                OR L78)) OR (L76 AND (L77 OR L78)) OR (L77 AND L78)

     FILE 'HCAPLUS' ENTERED AT 14:57:47 ON 22 SEP 2006
                D QUE L79
                D IBIB ABS L79 TOT

     FILE 'CAPLUS' ENTERED AT 14:58:01 ON 22 SEP 2006
                D QUE L70
L80         123 SEA ABB=ON  PLU=ON  L53 (L) (THU OR DMA OR PKT OR PAC OR
                BAC)/RL
L81          73 SEA ABB=ON  PLU=ON  L80 AND (PY<2001 OR AY<2001 OR PRY<2001)
L82          90 SEA ABB=ON  PLU=ON  (L81 OR L70)
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L83           62 SEA ABB=ON  PLU=ON  L81 AND L70
                 D QUE L83
                 D IBIB ABS HITSTR L83 32-62


=> file hcaplus
FILE 'HCAPLUS' ENTERED AT 14:57:47 ON 22 SEP 2006
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FILE COVERS 1907 - 22 Sep 2006  VOL 145 ISS 14
FILE LAST UPDATED: 21 Sep 2006  (20060921/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d que l79
L71           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("LIVNAH N"/AU OR "LIVNAH
                 NURIT"/AU)
L72           16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("YECHEZKEL T"/AU OR "YECHEZKE
                 L TAMAR"/AU)
L73           11 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("SALITRA Y"/AU OR "SALITRA
                 YOSEF"/AU OR "SALITRA YOSEPH"/AU OR "SALITRA YOSPHE"/AU OR
                 SALITRE/AU)
L74            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("PERLMUTTER B"/AU OR
                 "PERLMUTTER B H"/AU OR "PERLMUTTER BORIS"/AU)
L75            3 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("OHNE O"/AU OR "OHNE
                 ONSAT"/AU OR "OHNE OSNAT"/AU)
L76          553 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ("COHEN I"/AU OR "COHEN I
                 A"/AU OR "COHEN I BERNARD"/AU OR "COHEN I C"/AU OR "COHEN I
                 E"/AU OR "COHEN I J"/AU OR "COHEN I K"/AU OR "COHEN I KELMAN"/A
                 U OR "COHEN I L"/AU OR "COHEN I M"/AU OR "COHEN I R"/AU OR
                 "COHEN I RANDELL"/AU OR "COHEN I ROY"/AU OR "COHEN I S"/AU OR
                 "COHEN ILAN"/AU OR "COHEN ILANA"/AU)
L77           13 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "LITMAN PNINIT"/AU
L78           35 SEA FILE=HCAPLUS ABB=ON  PLU=ON  "SENDEROWITZ HANOCH"/AU
L79            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L71 AND (L72 OR L73 OR L74
                 OR L75 OR L76 OR L77 OR L78)) OR (L72 AND (L73 OR L74 OR L75
                 OR L76 OR L77 OR L78)) OR (L73 AND (L74 OR L75 OR L76 OR L77
                 OR L78)) OR (L74 AND (L75 OR L76 OR L77 OR L78)) OR (L75 AND
                 (L76 OR L77 OR L78)) OR (L76 AND (L77 OR L78)) OR (L77 AND
                 L78)


=> d ibib abs l79 tot
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L79 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1124555 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 142:69212
TITLE: Cell-permeable conjugates of peptides for inhibition of protein kinases, pharmaceutical compositions, and therapeutic uses
INVENTOR(S): ***Livnah, Nurit***; Levitzki, Alexander; Senderovitz, Hanoch; ***Yechezkel, Tamar***; ***Salitra, Yosef***; ***Litman, Pninit***; ***Ohne, Osnat***
PATENT ASSIGNEE(S): Develogen Israel Ltd., Israel
SOURCE: PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110337	A2	20041223	WO 2004-IL505	20040613
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004246894	A1	20041223	AU 2004-246894	20040613
EP 1646352	A2	20060419	EP 2004-736727	20040613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				

PRIORITY APPLN. INFO.: IL 2003-156429 A 20030612
WO 2004-IL505 W 20040613

OTHER SOURCE(S): MARPAT 142:69212

AB The invention provides inhibitors of protein kinases comprising a mol. having at least a first moiety competent for penetration of the mol. into cells, and a second moiety for having a protein kinase-inhibiting effect within the cells, the first moiety being joined to the second moiety through a linker or a spacer. The complex mols. of the invention are preferably peptide conjugates having improved cell permeability, serum stability, and kinase selectivity compared to known protein kinase inhibitors. Pharmaceutical compns. comprising these protein kinase inhibitors, and methods of using such compns. for treatment of cancers and other diseases associated with protein kinase activity are also disclosed.

L79 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:777516 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 139:288310
TITLE: Photo-active backbone cyclized somatostatin analogs for photodynamic therapy and imaging
INVENTOR(S): Bonasera, Thomas A.; ***Livnah, Nurit***; ***Salitra, Yoseph***; ***Yechezkel, Tamar***
PATENT ASSIGNEE(S): Peptor, Ltd., Israel

SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003079966	A2	20031002	WO 2003-IL239	20030319
WO 2003079966	A3	20040506		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003216703	A1	20031008	AU 2003-216703	20030319
EP 1494694	A2	20050112	EP 2003-712617	20030319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005090429	A1	20050428	US 2004-950378	20040924
PRIORITY APPLN. INFO.:			IL 2002-148921 A	20020326
			WO 2003-IL239 W	20030319

AB Novel photo-active labeled diagnostic and therapeutic peptides which are conformationally constrained backbone cyclized somatostatin analogs, having improved somatostatin receptor subtype affinity and selectivity are disclosed. The backbone cyclized peptide analogs disclosed possess unique and superior properties over other analogs, such as chemical and metabolic stability, selectivity, increased bioavailability and improved pharmacokinetics. Furthermore, the unique patterns of receptor subtype selectivity provide compds. having improved diagnostic and therapeutic utilities. Pharmaceutical compns. comprising the photo-active backbone cyclized somatostatin analogs, reagents for synthesizing same, and methods of using such compns. for diagnostic and therapeutic purposes including optical imaging and photodynamic therapy are also disclosed.

L79 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:97516 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 138:147683
TITLE: Protein kinase inhibitors comprising ATP mimetics conjugated to peptides or peptidomimetics
INVENTOR(S): ***Livnah, Nurit; Yechezkel, Tamar; Salitra, Yosef; Perlmutter, Boris; Ohne, Onsat; Cohen, Ilana; Litman, Pninit; Senderowitz, Hanoch***
PATENT ASSIGNEE(S): Peptor Ltd., Israel
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003010281	A2	20030206	WO 2002-IL618	20020725
WO 2003010281	A3	20031113		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2455602	AA	20030206	CA 2002-2455602	20020725
EP 1416934	A2	20040512	EP 2002-751604	20020725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005501047	T2	20050113	JP 2003-515632	20020725
US 2005026840	A1	20050203	US 2004-764288	20040123
PRIORITY APPLN. INFO.:			IL 2001-144583 A	20010726
			WO 2002-IL618 W	20020725

OTHER SOURCE(S): MARPAT 138:147683

AB The present invention provides small mols. having high affinity to the ATP binding site of protein kinases, which are conjugated to a peptide or peptidomimetic moiety which mimics the substrate of PKB. The chimeric compds. (Markushes included) according to the present invention preferably serve as PKB inhibitors with improved activity and selectivity. Novel ATP mimetic compds. , particularly isoquinoline derivs., conjugated with peptides or peptidomimetics are useful as inhibitors of protein kinases for exptl., medical, and drug design purposes. Furthermore, pharmaceutical compns. comprising these protein kinase inhibitors, and methods of using such compns. for treatment and diagnosis of cancers, diabetes, cardiovascular pathologies, hemorrhagic shock, obesity, inflammatory diseases, diseases of the central nervous system, and autoimmune disease, are disclosed.

L79 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:615640 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 137:165559
TITLE: Backbone cyclized radiolabelled somatostatin analogs
INVENTOR(S): Bonasera, Thomas A.; ***Livnah, Nurit***; ***Yechezkel, Tamar***; ***Salitra, Yoseph***
PATENT ASSIGNEE(S): Peptor Ltd., Israel
SOURCE: PCT Int. Appl., 104 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062819	A2	20020815	WO 2002-IL91	20020204
WO 2002062819	A3	20030925		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,				

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002230063	A1	20020819	AU 2002-230063	20020204
US 2004102364	A1	20040527	US 2003-634496	20030804
PRIORITY APPLN. INFO.:			IL 2001-141276 A	20010205
			WO 2002-IL91 W	20020204

OTHER SOURCE(S): MARPAT 137:165559

AB Novel radiodiagnostic and radiotherapeutic peptides which are conformationally constrained backbone cyclized somatostatin analogs, having improved somatostatin receptor subtype affinity and selectivity are disclosed. The backbone cyclized peptide analogs disclosed posses unique and superior properties over other analogs, such as chemical and metabolic stability, selectivity, increased bioavailability and improved pharmacokinetics. Furthermore, the unique patterns of receptor subtype selectivity provide compds. having improved diagnostic and therapeutic utilities. Pharmaceutical compns. comprising the backbone cyclized somatostatin analogs and radiolabeled analogs, reagents for synthesizing same, and methods of using such compns. for radiodiagnostic and radiotherapeutic purposes are also disclosed.

L79 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:536576 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 137:241819
TITLE: Toward a PKB Inhibitor: Modification of a Selective PKA Inhibitor by Rational Design
AUTHOR(S): Reuveni, Hadas; ***Livnah, Nurit***; Geiger, Tamar; Klein, Shoshana; ***Ohne, Osnat***; ***Cohen, Ilana***; Benhar, Moran; Gellerman, Gary; Levitzki, Alexander
CORPORATE SOURCE: Department of Biological Chemistry, The Silverman Institute of Life Sciences, Hebrew University of Jerusalem, Jerusalem, Israel
SOURCE: Biochemistry (2002), 41(32), 10304-10314
CODEN: BICHAW; ISSN: 0006-2960
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Protein kinase B/Akt (PKB) is an anti-apoptotic protein kinase that has strongly elevated activity in human malignancies. We therefore initiated a program to develop PKB inhibitors, "Aktstatins". We screened about 500 compds. for PKB inhibitors, using a radioactive assay and an ELISA assay that we established for this purpose. These compds. were produced as combinatorial libraries, designed using the structure of the selective PKA inhibitor H-89 as a starting point. We have identified a successful lead compound, which inhibits PKB activity in vitro and in cells overexpressing active PKB. The new compound shows reversed selectivity to H-89: In contrast to H-89, which inhibits PKA 70 times better than PKB, the new compound, NL-71-101, inhibits PKB 2.4-fold better than PKA. The new compound, but not H-89, induces apoptosis in tumor cells in which PKB is amplified. We have identified structural features in NL-71-101 that are significant for the specificity and that can be used for future development and optimization of PKB inhibitors.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:827035 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 136:210716
TITLE: A bicyclic and Hsst2 selective somatostatin analogue: design, synthesis, conformational analysis and binding
AUTHOR(S): Falb, Eliezer; ***Salitra, Yoseph***; ***Yechezkel, Tamar***; Bracha, Moshe; ***Litman, Pninit***; Olender, Roberto; Rosenfeld, Rakefet; ***Senderowitz, Hanoch***; Jiang, Shaokai; Goodman, Murray
CORPORATE SOURCE: Peptor Ltd., Rehovot, 76326, Israel
SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(12), 3255-3264
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A backbone bridged and disulfide bridged bicyclic somatostatin analog, compound 1 (PTR-3205), was designed and synthesized by solid-phase methodol. The binding of compound 1 to the five different somatostatin receptors, expressed in CHO or COS-7 cells, indicate a high degree of selectivity towards hsstr2. The three-dimensional structure of this compound has been determined in DMSO-d6 and in water by 1H NMR and by mol. dynamics simulations. Similar backbone conformations were observed in both solvents. The authors have established direct evidence that the backbone of this bicyclic somatostatin analog assumes a 'folded' conformation in solution, where the lactam ring extends roughly in the plane of the β-turn. The pharmacophoric region Phe-(d)-Trp-Lys-Thr of compound 1 is in accord with that of both the Veber compound L-363,301 (Merck) and sandostatin. The authors believe that the enhanced selectivity towards the hsst2 receptor, in comparison with other analogs, is due to its large hydrophobic region, composed of the lactam ring and the Phe side chains at positions 1 and 8.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:894549 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 134:208088
TITLE: In situ generation of Fmoc amino acid chlorides for extremely difficult couplings to sterically hindered secondary amines in solid-phase peptide synthesis
AUTHOR(S): Falb, Eliezer; ***Yechezkel, Tamar***; ***Salitra, Yosphe***; Gellerman, Gary; Muller, Dan; Gilon, Chaim
CORPORATE SOURCE: Peptor Ltd., Rehovot, 76326, Israel
SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 55-57. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Bis(trichloromethyl)carbonate (BTC) is used to generate, in-situ, Fmoc-amino acid chlorides for their use in difficult peptide coupling reactions in solid-phase peptide synthesis.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:53668 HCAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 132:108301
TITLE: Processes for coupling amino acids using bis(trichloromethyl) carbonate
INVENTOR(S): Falb, Eliezer; ***Yechezkel, Tamar***; ***Salitra, Yoseph***
PATENT ASSIGNEE(S): Peptor Ltd., Israel
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002898	A1	20000120	WO 1999-IL378	19990711
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
IL 125314	A1	20040725	IL 1998-125314	19980712
CA 2334076	AA	20000120	CA 1999-2334076	19990711
AU 9946454	A1	20000201	AU 1999-46454	19990711
AU 754560	B2	20021121		
EP 1097164	A1	20010509	EP 1999-929678	19990711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002520331	T2	20020709	JP 2000-559127	19990711
NZ 509304	A	20030131	NZ 1999-509304	19990711
CZ 296014	B6	20051214	CZ 2001-159	19990711
US 2001007037	A1	20010705	US 2001-756223	20010109
US 6512092	B2	20030128		
ZA 2001000370	A	20010726	ZA 2001-370	20010112
US 2003195331	A1	20031016	US 2002-321648	20021218
US 7045592	B2	20060516		

PRIORITY APPLN. INFO.:
IL 1998-125314 A 19980712
WO 1999-IL378 W 19990711
US 2001-756223 A3 20010109

OTHER SOURCE(S): CASREACT 132:108301

AB A process is disclosed for using triphosgene as an efficient and effective coupling reagent during peptide synthesis, by in situ generation of amino acid chloride from a protected amino acid. This process is particularly useful for the coupling to sterically hindered amino acid residues or for other difficult couplings. Furthermore, the same reagent can be used for the derivatization of peptides by formation of an amide bond between a free amine on a peptide and a carboxylic acid or for the coupling of an amino acid to a solid support. Results for difficult peptide couplings using triphosgene are tabulated.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L79 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:383559 HCAPLUS <<LOGINID::20060922>>

DOCUMENT NUMBER: 131:157968
TITLE: In situ generation of Fmoc-amino acid chlorides using bis-(trichloromethyl)carbonate and its utilization for difficult couplings in solid-phase peptide synthesis
AUTHOR(S): Falb, E.; ***Yechezkel, T.***; ***Salitra, Y.***; Gilon, C.
CORPORATE SOURCE: Peptor Ltd, Kiryat Weizmann, Rehovot, 76326, Israel
SOURCE: Journal of Peptide Research (1999), 53(5), 507-517
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper reports utilizing bis(trichloromethyl)carbonate (BTC) to generate, in situ, Fmoc-amino acid chlorides for their use in difficult coupling reactions during solid-phase peptide synthesis. The BTC-mediated coupling of all Fmoc-protected proteinogenic amino acids to a large variety of N-alkylated amino acid-peptidyl-resin was studied. The majority of the couplings proceeded with quant. conversion and without racemization. The utilization of BTC-mediated coupling for facile solid-phase synthesis of backbone cyclic peptides is presented.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE LAST UPDATED: 21 Sep 2006 (20060921/ED)

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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                -7/BI OR 494824-91-8/BI OR 56-65-5/BI)
L7          225 SEA FILE=REGISTRY SSS FUL L1
L12           7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L4 NOT L7
L13           4 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND SQL/FA
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

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L29           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  147318-81-8
L52         228 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 NOT 147318-81-8
L53           1 SEA FILE=REGISTRY ABB=ON  PLU=ON  L14 NOT L52
L54          95 SEA FILE=CAPLUS ABB=ON  PLU=ON  L52
L56         153 SEA FILE=CAPLUS ABB=ON  PLU=ON  L53
L57         129 SEA FILE=CAPLUS ABB=ON  PLU=ON  L56 NOT L54
L59         205 SEA FILE=REGISTRY ABB=ON  PLU=ON  L26 NOT 147318-81-8
L60          86 SEA FILE=CAPLUS ABB=ON  PLU=ON  L59
L61         129 SEA FILE=CAPLUS ABB=ON  PLU=ON  L27 NOT L60
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                PRY<2001)
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L66         153 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L56 OR L65)
L67         129 SEA FILE=CAPLUS ABB=ON  PLU=ON  L66 NOT L54
L68         129 SEA FILE=CAPLUS ABB=ON  PLU=ON  (L57 OR L67)
L69          79 SEA FILE=CAPLUS ABB=ON  PLU=ON  L68 AND (PY<2001 OR AY<2001 OR
                PRY<2001)
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                PAC OR BAC)/RL
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                PRY<2001)
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L83  ANSWER 32 OF 62  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1998:548898  CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER:          129:270036
TITLE:                    Relative potency of protease inhibitors in
                          monocytes/macrophages acutely and chronically infected
                          with human immunodeficiency virus
AUTHOR(S):                Perno, Carlo-Federico; Newcomb, Fonda M.; Davis, David
                          A.; Aquaro, Stefano; Humphrey, Rachel W.; Calio,
                          Raffaele; Yarchoan, Robert
CORPORATE SOURCE:         HIV and AIDS Malignancy Branch, Natl. Cancer Inst.,
                          Natl. Inst. Health, Bethesda, MD, USA
SOURCE:                   Journal of Infectious Diseases (1998),
                          178(2), 413-422
                          CODEN: JIDIAQ; ISSN: 0022-1899
PUBLISHER:                University of Chicago Press
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
```

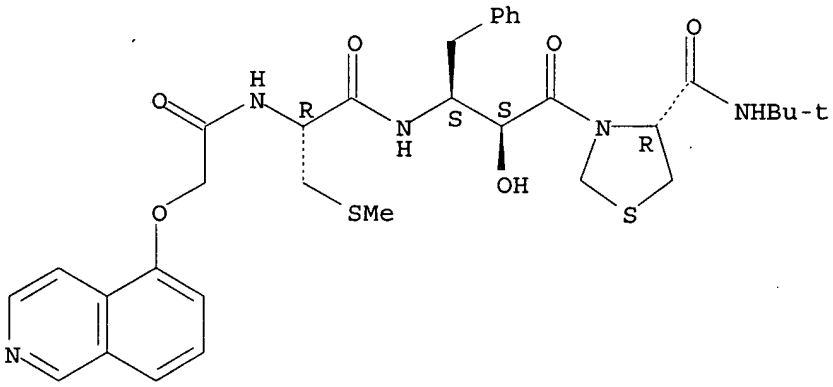
AB The activity of three human immunodeficiency virus (HIV) protease inhibitors was investigated in human primary monocytes/macrophages (M/M) chronically infected by HIV-1. Saquinavir, KNI-272, and ritonavir inhibited the replication of HIV-1 in vitro, with EC50s of .apprx.0.5-3.3 μM. However, only partial inhibition was achievable, even at the highest concns. tested. Also, the activity of these drugs in chronically infected M/M was .apprx.7- to 26-fold lower than in acutely infected M/M and .apprx.2- to 10-fold lower than in chronically infected H9 lymphocytes. When protease inhibitors were removed from cultures of chronically infected M/M, production of virus rapidly returned to the levels found in untreated M/M. Therefore, relatively high concns. of protease inhibitors are required to suppress HIV-1 production in chronically infected macrophages, and such cells may be a vulnerable point for the escape of virus in patients taking these drugs.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(relative potency of protease inhibitors in monocytes/macrophages acutely and chronically infected with human immunodeficiency virus)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 71 THERE ARE 71 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 33 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:509110 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 129:104199
TITLE: Enhanced suppression of HIV-1 by the combination of cytidine nucleoside analogs and CTP synthase inhibitors
INVENTOR(S): Gao, Wen-yi; Johns, David G.; Mitsuya, Hiroaki; Marquez, Victor
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9831375	A1	19980723	WO 1998-US784	19980120 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9858255	A1	19980807	AU 1998-58255	19980120 <--
PRIORITY APPLN. INFO.:			US 1997-33918P	P 19970121 <--
			WO 1998-US784	W 19980120 <--

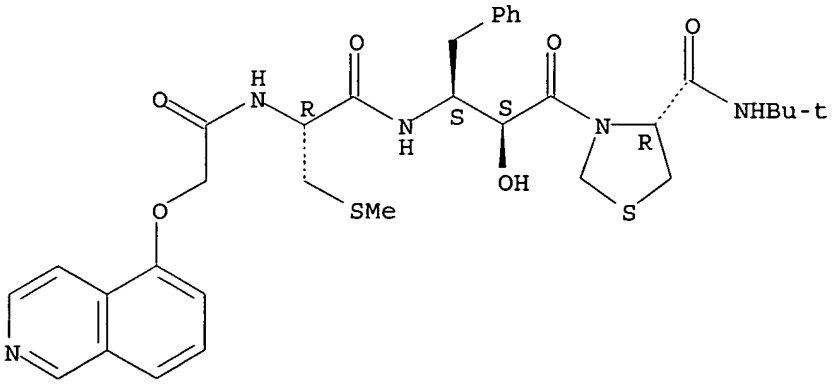
AB A method is disclosed to increase the potency of cytidine-based anti-HIV drugs using CTP synthase inhibitors, and to overcome resistance of human immunodeficiency virus (HIV) to cytidine-based anti-HIV drugs using CTP synthase inhibitors.

IT ***147318-81-8***, KNI272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(HIV resistant to; cytidine nucleoside analog-CTP synthase inhibitor combination for inhibition of retrovirus or virus using reverse transcriptase)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 34 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:501276 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 129:170511

TITLE: Use of quinoxalines in three-way combinations with protease inhibitors and reverse transcriptase inhibitors as a drug for treating AIDS and/or HIV infections

INVENTOR(S): Paessens, Arnold; Blunck, Martin; Riess, Guenter; Kleim, Joerg-Peter; Roesner, Manfred

PATENT ASSIGNEE(S): Bayer A.-G., Germany

SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19703131	A1	19980730	DE 1997-19703131	19970129 <--
CA 2278773	AA	19980730	CA 1998-2278773	19980115 <--
WO 9832442	A1	19980730	WO 1998-EP197	19980115 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9860940	A1	19980818	AU 1998-60940	19980115 <--
EP 977570	A1	20000209	EP 1998-905297	19980115 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
BR 9807523	A	20000321	BR 1998-7523	19980115 <--
JP 2001511124	T2	20010807	JP 1998-531540	19980115 <--
ZA 9800679	A	19980805	ZA 1998-679	19980128 <--
NO 9903670	A	19990910	NO 1999-3670	19990728 <--
MX 9907077	A	20000531	MX 1999-7077	19990729 <--
PRIORITY APPLN. INFO.:			DE 1997-19703131 A	19970129 <--
			WO 1998-EP197 W	19980115 <--

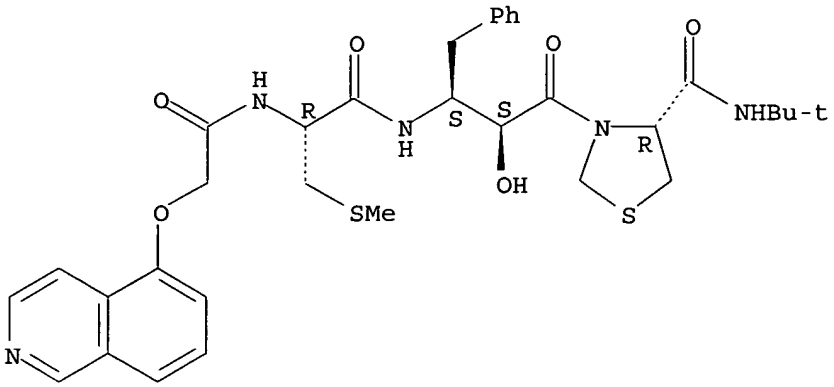
AB Quinoxaline derivs. in combination with protease inhibitors and reverse transcriptase inhibitors inhibited HIV replication in human lymphocytes. Such 3-way combinations are synergistic and may be used to treat persons with HIV infections or AIDS.

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(AIDS and HIV infections treatment by combinations of quinoxalines and reverse transcriptase inhibitors with protease inhibitors such as)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 35 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:496618 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 129:225321
TITLE: Flexibility and Function in HIV Protease: Dynamics of the HIV-1 Protease Bound to the Asymmetric Inhibitor Kynostatin 272 (KNI-272)
AUTHOR(S): Freedberg, Daron I.; Wang, Yun-Xing; Stahl, Stephen J.; Kaufman, Joshua D.; Wingfield, Paul T.; Kiso, Yoshiaki; Torchia, Dennis A.
CORPORATE SOURCE: Molecular Structural Biology Unit National Institute of Dental Research, National Institutes of Health, Bethesda, MD, 20892, USA
SOURCE: Journal of the American Chemical Society (*1998*), 120(31), 7916-7923
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The HIV-1 protease is a 22 kDa homodimeric protein essential for function of the AIDS virus, and protease inhibitors have been developed into effective HIV drugs. To better understand HIV-1 protease-inhibitor interactions, we have investigated amide backbone dynamics by correlated 1H-15N NMR spectroscopy. To date, HIV-1 protease/inhibitor complexes studied by NMR spectroscopy have been limited to C2 sym. structures, consisting of the protease bound to a sym. inhibitor. Herein we report studies of the dynamics of HIV-1 protease complexed to KNI-272, a potent (Ki 5 pM), asym. inhibitor which lifts the chemical shift degeneracy of the protease monomers and allows us to ascertain if the individual protease monomers have significantly different backbone motions. Using isotope filtered/edited spectra of 15N/13C protease complexed with unlabeled KNI-272, together with distances derived from the protease/KNI-272 x-ray structure, we obtained monomer specific NMR signal assignments. We derived information about monomer dynamics from a Lipari-Szabo anal. of amide 15N T1, T2, and NOE values. Modeling the complex as an axially sym. rotor yielded an average overall correlation time of 9.65 ns and an anisotropy, D||/D⊥, of 1.27. Over 90% of the backbone amide sites are highly ordered with the squared order parameter, averaged over all measured residues, being 0.85. High amplitude internal motions are observed in several loops in the protease, especially those in the elbows of the flaps, while millisecond to microsecond time scale motion is observed at the flap-tips. While these results are similar to those reported for

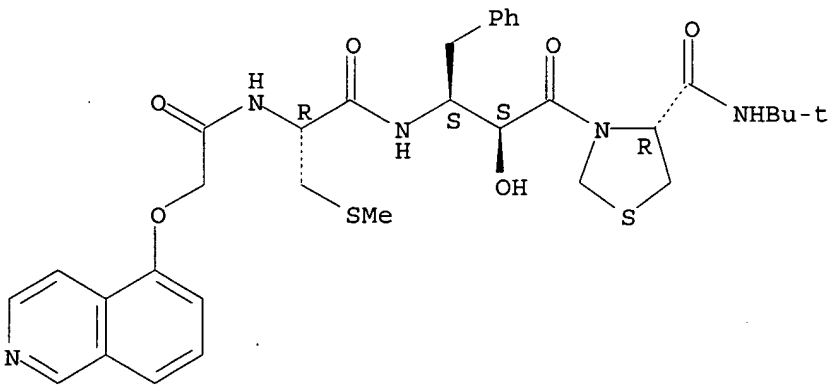
complexes with sym. inhibitors, we find differences in internal motions between several residues in the flap of one monomer and the corresponding residues on the other monomer. Residue Gly 149 has a significantly larger order parameter than Gly 49; in addition, the motions on the chemical exchange time scale contribute to the relaxation of Gly 152 and Phe 153 but not to the relaxation of Gly 52 and Phe 53. These differences in flexibility correlate with differences in interactions made by these residues with KNI-272, as seen in the crystal structure. We also find that the average of the order parameters measured for residues in monomer 1 is less than for monomer 2, a result that correlates with the observation that average B factor for these residues is less in monomer 2 than in monomer 1.

IT ***147318-81-8D***, KNI-272, complexes with HIV-1 protease
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ***THU (Therapeutic use)***; BIOL (Biological study); PROC (Process); USES (Uses)
(dynamics of HIV-1 protease bound to asym. inhibitor kynostatin 272 (KNI-272))

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 36 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:436588 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 129:117415
TITLE: Pharmacokinetics of the protease inhibitor KNI-272 in plasma and cerebrospinal fluid in nonhuman primates after intravenous dosing and in human immunodeficiency virus-infected children after intravenous and oral dosing
AUTHOR(S): Mueller, Brigitta U.; Anderson, Barry D.; Farley, Maureen Q.; Murphy, Robert; Zuckerman, Judy; Jarosinski, Paul; Godwin, Karen; McCully, Cindy L.; Mitsuya, Hiroaki; Pizzo, Philip A.; Balis, Frank M.
CORPORATE SOURCE: Pediatric Branch, National Cancer Institute, Pharmacy Department, National Institutes Health, Bethesda, MD, 20892, USA

SOURCE: Antimicrobial Agents and Chemotherapy (*1998*), 42(7), 1815-1818
CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

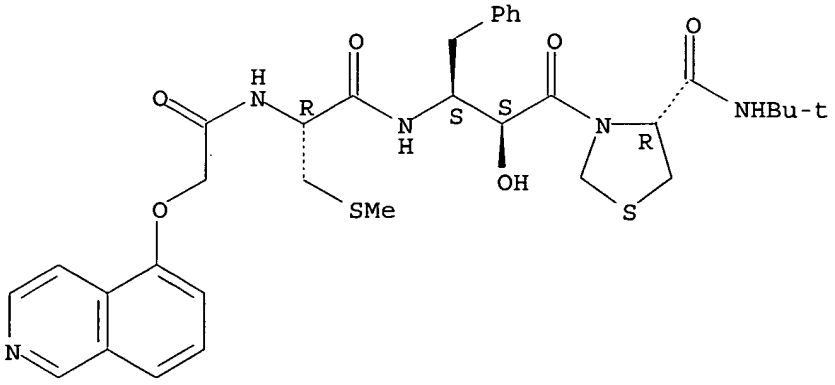
AB KNI-272 is a human immunodeficiency virus (HIV) protease inhibitor with potent activity in vitro. We studied the pharmacokinetics of KNI-272 in the plasma and cerebrospinal fluid (CSF) of a nonhuman primate model and after i.v. and oral administration to children with HIV infection. Plasma and CSF were sampled over 24 h after the administration of an i.v. dose of 50 mg of KNI-272 per kg of body weight (approx. 1,000 mg/m2) to three nonhuman primates. The pharmacokinetics of KNI-272 were also studied in 18 children (9 males and 9 females; median age, 9.4 yr) enrolled in a phase I trial of four dose levels of KNI-272 (100, 200, 330, and 500 mg/m2 per dose given four times daily). The plasma concentration-time profile of KNI-272 in the nonhuman primate model was characterized by considerable inter-animal variability and rapid elimination (clearance, 2.5 L/h/kg; terminal half-life, 0.54 h). The level of drug exposure achieved in CSF, as measured by the area under the KNI-272 concentration-time curve, was only 1% of that achieved in plasma. The pharmacokinetics of KNI-272 in children were characterized by rapid elimination (clearance, 276 mL/min/m2; terminal half-life, 0.44 h), limited (12%) and apparently saturable bioavailability, and limited distribution (volume of distribution at steady state, 0.11 L/kg). The concns. in plasma were maintained above a concentration that is active in vitro for less than half of the 6-h dosing interval. There was no significant increase in CD4 cell counts or decrease in p24 antigen or HIV RNA levels. The pharmacokinetic profile of KNI-272 may limit the drug's efficacy in vivo. It appears that KNI-272 will play a limited role in the treatment of HIV-infected children.

IT ***147318-81-8***, KNI-272
RL: BPR (Biological process); BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); PROC (Process); USES (Uses)
(protease inhibitor KNI-272 i.v. and oral pharmacokinetics in plasma and cerebrospinal fluid of nonhuman primates and HIV-infected children)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 37 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:351758 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 129:45325
TITLE: Liquid pharmaceutical compositions containing HIV protease inhibitors
INVENTOR(S): Lipari, John; Al-Razzak, Laman A.; Ghosh, Soumojeet; Gao, Rong; Kaul, Dilip
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9822106	A1	19980528	WO 1997-US20794	19971112 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ZA 9710071	A	19980525	ZA 1997-10071	19971107 <--
CA 2271196	C	19980528	CA 1997-2271196	19971112 <--
CA 2271196	AA	19980528		
CA 2505430	AA	19980528	CA 1997-2505430	19971112 <--
AU 9852573	A1	19980610	AU 1998-52573	19971112 <--
AU 717546	B2	20000330		
EP 942721	A1	19990922	EP 1997-947510	19971112 <--
EP 942721	B1	20030122		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI, RO				
CN 1248914	A	20000329	CN 1997-199780	19971112 <--
BR 9714310	A	20000502	BR 1997-14310	19971112 <--
JP 2000515555	T2	20001121	JP 1998-523751	19971112 <--
JP 3592337	B2	20041124		
TR 9901129	T2	20010521	TR 1999-1129	19971112 <--
NZ 335002	A	20010831	NZ 1997-335002	19971112 <--
EP 1283041	A1	20030212	EP 2002-11533	19971112 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
AT 231393	E	20030215	AT 1997-947510	19971112 <--
PT 942721	T	20030630	PT 1997-947510	19971112 <--
IL 129300	A1	20030706	IL 1997-129300	19971112 <--
ES 2191862	T3	20030916	ES 1997-947510	19971112 <--
PL 190185	B1	20051130	PL 1997-336980	19971112 <--
SK 285022	B6	20060406	SK 1999-655	19971112 <--
TW 475895	B	20020211	TW 1997-86117136	19971117 <--
NO 9902427	A	19990720	NO 1999-2427	19990520 <--
KR 2000057169	A	20000915	KR 1999-704469	19990520 <--
BG 64411	B1	20050131	BG 1999-103425	19990521 <--

HK 1022441	A1	20031031	HK 2000-101651		20000317 <--
AU 757970	B2	20030313	AU 2000-39414		20000609 <--
JP 2004346077	A2	20041209	JP 2004-163024		20040601 <--
PRIORITY APPLN. INFO.:			US 1996-754390	A	19961121 <--
			AU 1998-52573	A3	19971112 <--
			CA 1997-2271196	A3	19971112 <--
			EP 1997-947510	A3	19971112 <--
			JP 1998-523751	A3	19971112 <--
			WO 1997-US20794	W	19971112 <--

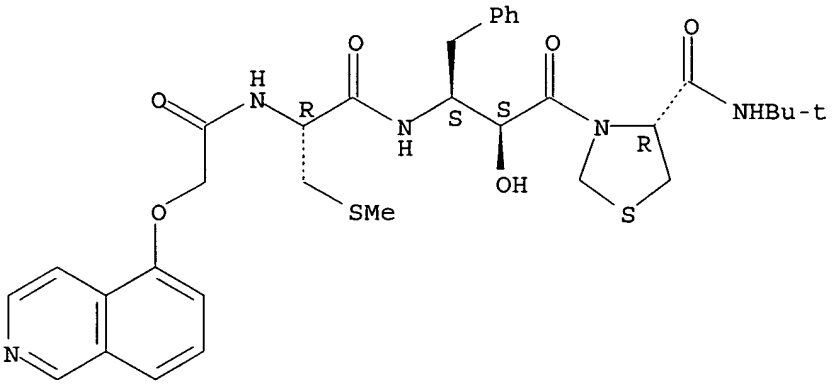
AB A liquid pharmaceutical composition providing improved oral bioavailability is disclosed for compds. which are inhibitors of HIV protease. In particular, the composition comprises a solution in a pharmaceutically acceptable organic solvent of (a) the HIV protease inhibitor and optionally, (b) a surfactant. The composition can optionally be encapsulated in either hard gelating capsules or soft elastic capsules (SEC). A capsule composition was prepared containing ritonavir 20, ethanol 10, oleic acid 69.99, and BHT 0.01% by weight

IT ***147318-81-8***
RL: ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(liquid pharmaceutical compns. containing HIV protease inhibitors)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 38 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1998:338135 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER:	128:326556
TITLE:	AIDS remedy
INVENTOR(S):	Sato, Hideharu; Shintani, Makoto; Fukazawa, Tominaga; Muto, Akihiro; Terajima, Keisuke
PATENT ASSIGNEE(S):	Japan Energy Corp., Japan
SOURCE:	PCT Int. Appl., 58 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9820888	A1	19980522	WO 1997-JP4057		19971107	<--
W: AU, CA, JP, NO, NZ, US						
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE						
CA 2270546	AA	19980522	CA 1997-2270546		19971107	<--
ZA 9710056	A	19980525	ZA 1997-10056		19971107	<--
AU 9748853	A1	19980603	AU 1997-48853		19971107	<--
AU 716760	B2	20000309				
EP 955054	A1	19991110	EP 1997-911479		19971107	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
NZ 335639	A	20010629	NZ 1997-335639		19971107	<--
NO 9902244	A	19990707	NO 1999-2244		19990507	<--
US 2002068749	A1	20020606	US 1999-297742		19990715	<--
PRIORITY APPLN. INFO.:			JP 1996-312772	A	19961108	<--
			JP 1996-344550	A	19961209	<--
			JP 1997-293365	A	19971009	<--
			WO 1997-JP4057	W	19971107	<--

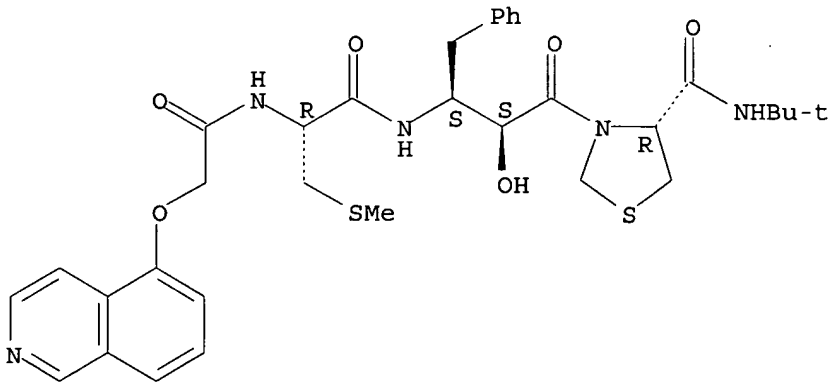
AB The invention relates to a medicinal composition which is suitable for administering a drug with an HIV protease inhibitory activity so as to achieve a higher remedial effect. The composition is an AIDS remedy which comprises KNI-272 and at least one compound, as the essential active ingredient having a human immunodeficiency virus protease inhibitory activity, selected from the group consisting of the compds. generally called saquinavir, ritonavir, indinavir, and nelfinavir. The KNI-272 and the active ingredient are contained in such a proportion and amts. as to produce a synergistic remedial effect.

IT ***147318-81-8***, KNI272
RL: ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(AIDS remedy)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



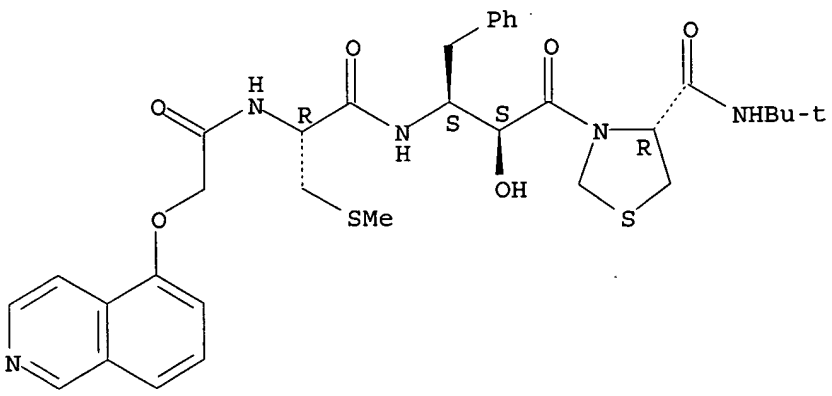
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 39 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:65902 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 128:123799
TITLE: Antiviral pharmaceutical compositions containing saturated 1,2-dithiaheterocyclic compounds, and uses thereof
INVENTOR(S): Rice, William G.; Schultz, Robert R.; Baker, David C.; Henderson, Louis E.
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; University of Tennessee Research Corp.
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9801440	A2	19980115	WO 1997-US10870	19970703 <--
WO 9801440	A3	19980514		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2260128	AA	19980115	CA 1997-2260128	19970703 <--
AU 9744085	A1	19980202	AU 1997-44085	19970703 <--
AU 737038	B2	20010809		
EP 1023284	A2	20000802	EP 1997-942372	19970703 <--
EP 1023284	B1	20051123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 310738	E	20051215	AT 1997-942372	19970703 <--
US 6046228	A	20000404	US 1999-214331	19990104 <--
PRIORITY APPLN. INFO.:			US 1996-21665P P	19960705 <--
			WO 1997-US10870 W	19970703 <--

OTHER SOURCE(S): MARPAT 128:123799
AB Pharmaceutical compns. including a saturated 1,2-dithiaheterocyclic compound having antiviral activity are provided. Also provided are a kit containing the pharmaceutical composition and methods of treating or preventing viral disease using the composition, as well as methods for inactivating a retrovirus in a body fluid.
IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(combination with; saturated dithiaheterocyclic compds. for antivirals, and pharmaceutical compns. containing them)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 40 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:780361 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 128:212774
TITLE: HIV-1 acquires resistance to two classes of antiviral drugs through homologous recombination
AUTHOR(S): Yusa, Keisuke; Kavlick, Mark F.; Kosalaraksa, Pope; Mitsuya, Hiroaki
CORPORATE SOURCE: Bethesda, Room, Bld. 10, National Cancer Institute, Division of Clinical Sciences, Medicine Branch, The Experimental Retrovirology Section, National Institutes of Health, MD 20892, 5A11, USA
SOURCE: Antiviral Research (*1997*), 36(3), 179-189
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Genetic recombination contributes to the genomic heterogeneity of human immunodeficiency virus type 1 (HIV-1). Here, the authors demonstrate that HIV-1 readily develops resistance to 2 classes of anti-HIV-1 drugs through in vitro genetic recombination involving large segments of the viral genome. Co-transfection of COS-7 cells with an HIV-1 plasmid (pSUM13) carrying 5 mutations in the reverse transcriptase (RT)-encoding region (A62V, V75I, F77L, F116Y, Q151M), conferring resistance to multiple dideoxynucleoside analogs (ddNs), and another HIV-1 plasmid (pSUM431) carrying 5 mutations in the protease-encoding region (V32I, L33F, K45I, I84V, L89M), conferring resistance to protease inhibitors such as KNI-272, readily produced HIV-1 carrying both sets of mutations when propagated in MT-2 cells in the presence of azidothymidine (AZT) and KNI-272. The resultant HIV-1 variant was highly resistant to both ddNs and KNI-272. Co-infection of MT-2 cells with HIV-1SUM13 carrying the RT mutations and HIV-1SUM431 carrying the mutations in the protease also generated HIV-1 with both sets of mutations when cultured with AZT and KNI-272. The authors also report here that the problematic artifactual recombination occurring during genetic analyses of heterogeneous nucleic acid sequences using polymerase chain reaction can be successfully obviated.

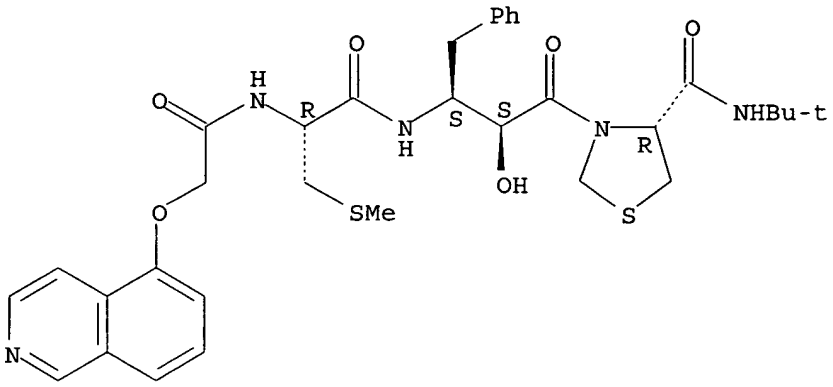
IT *147318-81-8*, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL

(Biological study); USES (Uses)
(HIV-1 acquires resistance to antiviral dideoxynucleoside analogs and protease inhibitors via homologous recombination)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 41 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:533533 CAPLUS <<LOGINID::20060922>>

DOCUMENT NUMBER: 127:215196

TITLE: Remedies or preventives for AIDS

INVENTOR(S): Komai, Tomoaki; Ohmine, Toshinori; Nishigaki, Takashi; Kimura, Tomio; Katsube, Tetsushi

PATENT ASSIGNEE(S): Sankyo Company, Ltd., Japan; Ube Industries, Ltd.

SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9727856	A1	19970807	WO 1997-JP218	19970130 <--
W: AU, CA, CN, CZ, HU, KR, MX, NO, NZ, RU, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2245179	AA	19970807	CA 1997-2245179	19970130 <--
AU 9715564	A1	19970822	AU 1997-15564	19970130 <--
AU 713704	B2	19991209		
EP 878194	A1	19981118	EP 1997-901785	19970130 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1214632	A	19990421	CN 1997-193373	19970130 <--
JP 09323932	A2	19971216	JP 1997-18078	19970131 <--
NO 9803512	A	19980930	NO 1998-3512	19980730 <--
PRIORITY APPLN. INFO.:			JP 1996-14825 A	19960131 <--

WO 1997-JP218 W 19970130 <--

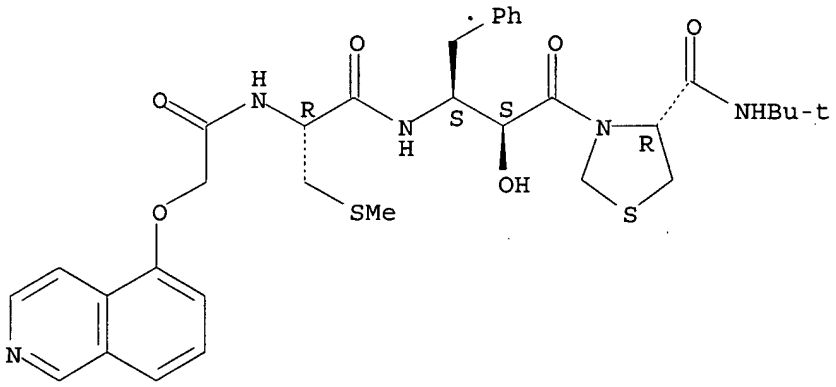
AB Combined use of one or more drugs selected from among quinolonecarboxylic acid-based anti-HIV agents with one or more drugs selected from among reverse transcriptase inhibitors and HIV protease inhibitors for treating or preventing AIDS; and remedies or preventives for AIDS containing as the active ingredient one or more drugs selected from among quinolonecarboxylic acid-based anti-HIV agents together with one or more drugs selected from among reverse transcriptase inhibitors and HIV protease inhibitors. Preparation and formulation examples are given.

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(quinolonecarboxylic acid derivs. as remedies or preventives for AIDS)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 42 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:446523 CAPLUS <<LOGINID::20060922>>

DOCUMENT NUMBER: 127:156263

TITLE: Conformational analysis of HIV-1 protease inhibitors. 2. Thioproline P'1 residue in the potent inhibitor KNI-272

AUTHOR(S): Murcko, Mark A.; Rao, B. Govinda; Gomperts, Roberto

CORPORATE SOURCE: Vertex Pharmaceuticals, Cambridge, MA, 02139-4242, USA

SOURCE: Journal of Computational Chemistry (***1997***), 18(9), 1151-1166
CODEN: JCCHDD; ISSN: 0192-8651

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The very potent HIV-1 protease (HIV-PR) inhibitor, KNI-272, contains a norstatine-thioproline linkage at P1-P'1. The three-dimensional crystal structure of this compound bound to HIV-PR has recently been determined [Baldwin et al., Structure, 3, 581 (1995)]. The crystal structure reveals a number of interesting interactions previously unseen in bound HIV-PR inhibitors.

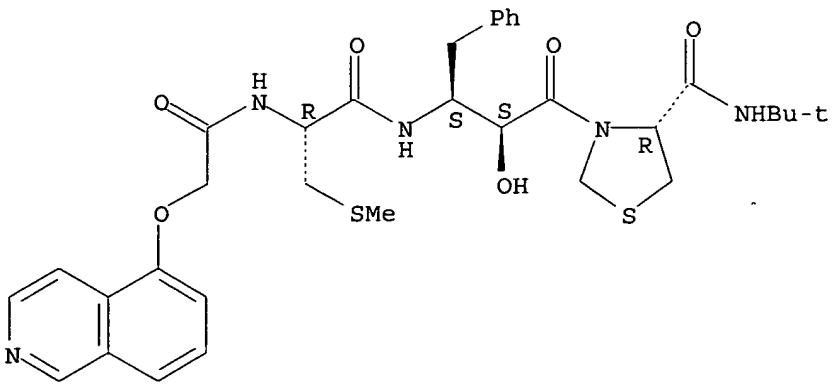
Here, the authors employ high-level ab initio calcns. and mol. modeling to ascertain the strain energy of the bound conformation of the norstatine-thioproline portion of KNI-272. Baldwin et al. suggested that two of the reasons for the high potency of KNI-272 are the rigidity of its backbone and a strong preference for the norstatine-thioproline amide linkage to adopt a trans conformation. The authors anal. shows that, on the contrary, there is still considerable flexibility in the backbone of the norstatine-based inhibitor. Furthermore, in the gas phase and in solution, there are both cis and trans conformations of the norstatine-thioproline amide linkage which are low in energy. However, when bound in the active site of HIV-PR, KNI-272 clearly has a strong preference for a trans conformation, which enables the formation of hydrogen bonds to the flap water. The authors calcns., at level up to MP2/6-31++G**//HF/6-31G*, suggest that the bound, trans amide conformation of the norstatine-thioproline "core" is still strained by 2-3 kcal/mol, primarily due to the placement of the P'1 thioproline carboxamide. This result is consistent with those previously obtained for the related protease inhibitor Ro 31-8959 (Saquinovir), which also requires a carboxamide to adopt a high-energy rotamer to preserve a good hydrogen bond to the flap water. However, the strain of the bound conformation of KNI-272 is clearly lower than that of Saquinovir. In addition, because the norstatine linkage does not contain a basic amine (as do Saquinovir and JG-365, for example), it should be easier to desolvate, which also assists in binding. The relation between KNI-272, JG-365, Saquinovir, and P'1 proline-containing substrate also is discussed.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(conformational anal. of HIV-1 protease inhibitors in relation to thioproline P'1 residue in potent inhibitor KNI-272)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 43 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:276427 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:246812

TITLE: Enhancement of the biological and antiviral activity of HIV protease inhibitors with macrolide and lincosamide antibiotics
INVENTOR(S): Schinazi, Raymond F.; Sommadossi, Jean-Pierre
PATENT ASSIGNEE(S): University of Alabama at Birmingham, USA; Schinazi, Raymond, F.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

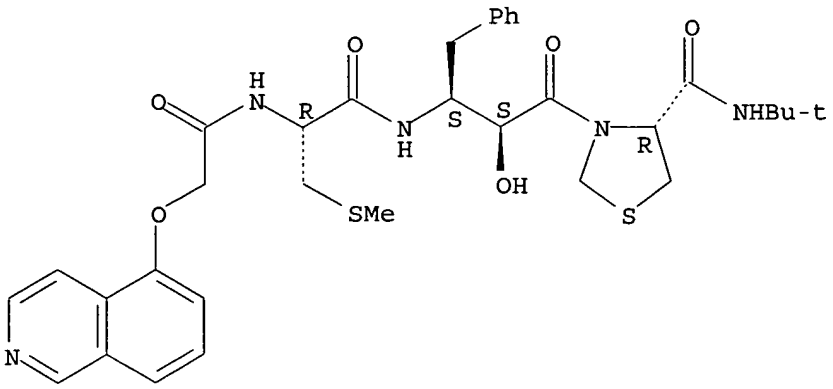
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9708180	A1	19970306	WO 1996-US13721		19960830	<--
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN						
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA						
US 5750493	A	19980512	US 1995-521474		19950830	<--
AU 9668601	A1	19970319	AU 1996-68601		19960830	<--
AU 716821	B2	20000309				
EP 876387	A1	19981111	EP 1996-929058		19960830	<--
EP 876387	B1	20051228				
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI						
JP 2001500471	T2	20010116	JP 1997-510502		19960830	<--
AT 314116	E	20060115	AT 1996-929058		19960830	<--
PRIORITY APPLN. INFO.:			US 1995-521474	A	19950830	<--
			WO 1996-US13721	W	19960830	<--

AB The cellular uptake of protease inhibitors (e.g. HIV protease inhibitor), in antiviral therapy based on inhibition of a protease required for viral maturation, is diminished by binding of the protease inhibitor to α1-acid glycoprotein (AAG), an acute-phase protein in serum. This effect is reversed, and the antiviral effectiveness of the protease inhibitors is restored, by coadministration of ≥1 AAG-binding compound, such as a macrolide or lincosamide antibiotic, which has sufficient binding affinity for AAG to competitively bind AAG in the presence of the protease inhibitor. Thus, cellular accumulation of HIV protease inhibitor SC-52151 by phytohemagglutinin-stimulated human peripheral blood mononuclear cells in the presence of AAG (1 mg/mL) was completely restored (to the level observed in the absence of AAG) by addition of erythromycin to 500 μM.

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(enhancement of biol. and antiviral activity of HIV protease inhibitors with macrolide and lincosamide antibiotics)

RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

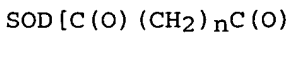
Absolute stereochemistry.



L83 ANSWER 44 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:262222 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:272344
TITLE: Antiviral drugs and their enhancers against HIV
INVENTOR(S): Nakajima, Hideki; Yamada, Kaneo; Igarashi, Toshisato
PATENT ASSIGNEE(S): Samu Kenkyusho Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09059178	A2	19970304	JP 1995-240947	19950824 <--
PRIORITY APPLN. INFO.:			JP 1995-240947	19950824 <--

GI



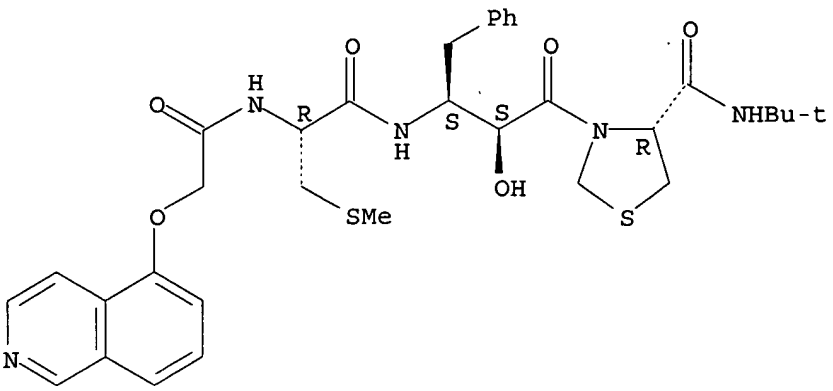
AB Antiviral formulations contain lecithin-binding human Cu,Zn-SOD (I; X = lyso-lecithin with 2-hydroxy at glycerol; m >1; n >2), HIV reverse transcriptase inhibitors (AZT, ddC, and ddI), HIV protease inhibitors (e.g. KNI-272), and/or sulfated polysaccharides (e.g. dextran sulfate). Thus, I was prepared from human-derived SOD and 2-(4-hydroxycarbonylbytyloyl)lyso-lecithin, and antiviral injections containing I and other antiviral agents were formulated. I in combination with AZT, ddC, ddI, KNI-272, or dextran sulfate had synergistic antiviral actions against HIV.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(antiviral drugs and their enhancers against HIV)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



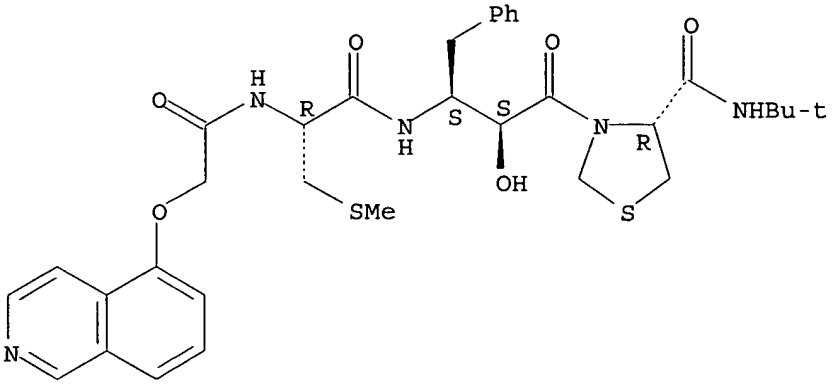
L83 ANSWER 45 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:222515 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:258544
TITLE: Lecithinized superoxide dismutase: an inhibitor of human immunodeficiency virus replication
AUTHOR(S): Premanathan, Mariappan; Nakashima, Hideki; Igarashi, Rie; Mizushima, Yutaka; Yamada, Kaneo
CORPORATE SOURCE: Department of Microbiology and Immunology, Kagoshima University School of Dentistry, Kagoshima, 890, Japan
SOURCE: AIDS Research and Human Retroviruses (*1997*), 13(4), 283-290
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Liebert
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Superoxide dismutase (SOD) is an enzyme used in the treatment of oxygen radical-related diseases. Lecithinization of SOD enhances its pharmacol. activity. Lecithinized SOD (PC-SOD) inhibits human immunodeficiency virus (HIV) types 1 and 2 in MT-4 cells. HIV-1-infected MT-4 cells were cultured for 5 days in the presence of PC-SOD, at various concns. In an MTT assay, reverse transcriptase (RT) activity of the cell extract and p24 antigen production were measured. Untreated, HIV-1-infected MT-4 cells served as control. PC-SOD inhibited viral replication most effectively at 2500 U/mL, a concentration that did not affect cell viability, with an EC50 value of 718 U/mL. PC-SOD treatment inhibited RT activity and p24 production in a dose-dependent manner. Western blot anal. of the HIV-1-infected MT-4 cells treated with PC-SOD at 2500 U/mL did not detect any expression of viral proteins. Failure to inhibit virus adsorption, proviral DNA and mRNA synthesis, and RT and proteinase enzyme activity suggests that the mechanism of action of PC-SOD is entirely different from those of the currently available anti-HIV drugs. PC-SOD shows synergistic interaction with AZT, ddI, ddC, KNI-272, and dextran sulfate. PC-SOD also inhibited the oxidative stress-induced depletion of sulfhydryls, which are the cause of diminished antioxidant defenses in HIV-infected patients.

IT ***147318-81-8***, KNI-272

RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(interaction of lecithinized superoxide dismutase and anti-HIV drugs)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 46 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:184660 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:166463
TITLE: Use of ritonavir (ABT-538) for improving the pharmacokinetics of drugs metabolized by cytochrome P450 in a method of treating aids
INVENTOR(S): Norbeck, Daniel W.; Kempf, Dale J.; Leonard, John M.; Bertz, Richard J.
PATENT ASSIGNEE(S): Abbott Laboratories, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9701349	A1	19970116	WO 1996-US11015	19960628 <--
W: AU, CA, IS, JP, KR, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6037157	A	20000314	US 1996-687774	19960626 <--
CA 2224738	AA	19970116	CA 1996-2224738	19960628 <--
CA 2224738	C	20020827		
AU 9663420	A1	19970130	AU 1996-63420	19960628 <--
AU 722812	B2	20000810		
EP 871465	A1	19981021	EP 1996-922604	19960628 <--
EP 871465	B1	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 11508884	T2	19990803	JP 1997-504572	19960628 <--

EP 1210941	A2	20020605	EP 2001-204308	19960628 <--
EP 1210941	A3	20020731		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 225186	E	20021015	AT 1996-922604	19960628 <--
EP 1273298	A2	20030108	EP 2002-79002	19960628 <--
EP 1273298	A3	20030319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
EP 1284140	A2	20030219	EP 2002-79003	19960628 <--
EP 1284140	A3	20030319		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
EP 1293207	A1	20030319	EP 2002-79004	19960628 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
ES 2186787	T3	20030516	ES 1996-922604	19960628 <--
HK 1016088	A1	20030808	HK 1999-101376	19990407 <--
AU 759386	B2	20030410	AU 2000-56443	20000904 <--
US 2002039998	A1	20020404	US 2001-957171	20010920 <--
US 6703403	B2	20040309		

PRIORITY APPLN. INFO.:	US 1995-654P	P	19950629 <--
	US 1995-3849P	P	19950915 <--
	US 1996-687774	A3	19960626 <--
	AU 1996-63420	A3	19960628 <--
	EP 1996-922604	A3	19960628 <--
	WO 1996-US11015	W	19960628 <--
	US 1999-387261	A3	19990831 <--

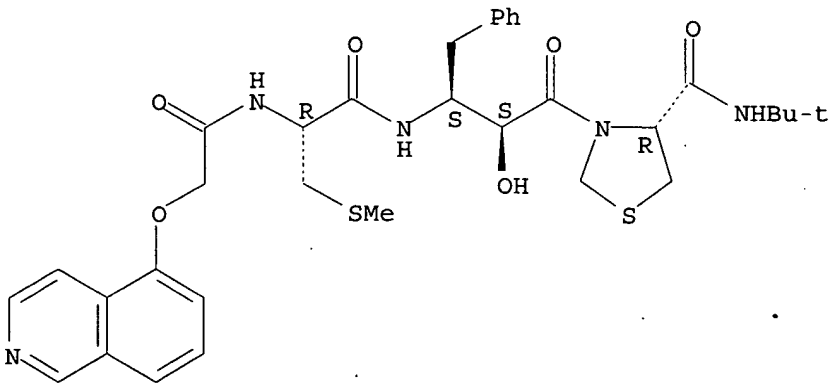
AB A method is disclosed for improving the pharmacokinetics of a drug which is metabolized by cytochrome P 450 monooxygenase by use of ritonavir. HIV inhibitory action is also claimed by combinations of ritonavir with protease inhibitors whose pharmacokinetics are modulated by ritanovir via its inhibitory action on cytochrome P 450.

IT ***147318-81-8***, Kni 272
RL: ***BAC (Biological activity or effector, except adverse)***; BPR (Biological process); BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); PROC (Process); USES (Uses)
(ritonavir inhibits P 450 and modulates drug pharmacokinetics and combined HIV antiviral action with protease inhibitors)

RN 147318-81-8 CAPLUS

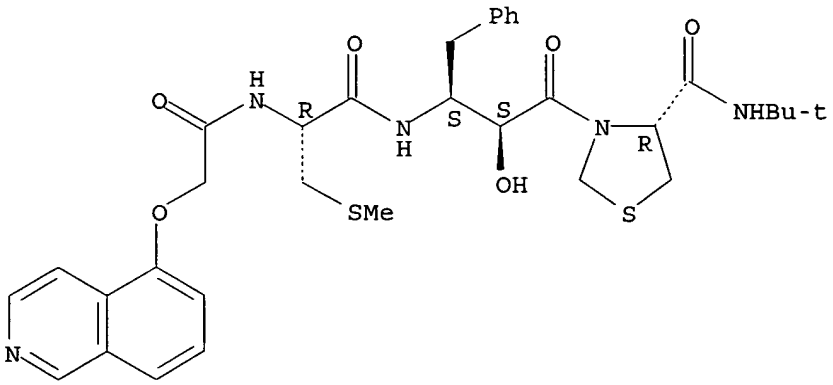
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 47 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:30148 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:69590
TITLE: KNI-272. Kynostatin-272. Antiviral for AIDS. HIV-1 protease inhibitor
AUTHOR(S): Ireland, C. D.; Castaner, J.
CORPORATE SOURCE: Prous Science Publishers, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (***1996***), 21(10), 1022-1027
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 41 refs., describing the synthesis, antiviral activity, pharmacokinetics, toxicity, and clin. uses of the title drug.
IT ***147318-81-8P***, Kynostatin 272
RL: ADV (Adverse effect, including toxicity); ***BAC (Biological activity or effector, except adverse)***; BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); ***THU (Therapeutic use)***; BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(Kynostatin 272; preparation and antiviral pharmacol. of)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 48 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:693923 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:114991
TITLE: Expression, characterization, and mutagenesis of the aspartic proteinase from equine infectious anemia virus
AUTHOR(S): Powell, David J.; Bur, Daniel; Wlodawer, Alexander; Gustchina, Alla; Payne, Susan L.; Dunn, Ben M.; Kay, John
CORPORATE SOURCE: College Cardiff, Univ. Wales, Cardiff, CF1 3US, UK

SOURCE: European Journal of Biochemistry (*1996*), 241(2), 664-674
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

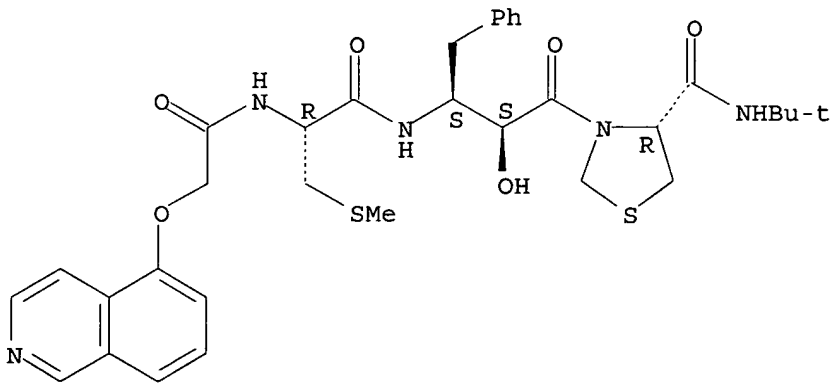
AB The gene encoding the proteinase from equine infectious anemia virus (EIAV) was cloned and expressed in Escherichia coli. The recombinant EIAV proteinase was purified to homogeneity and shown to have the ability to process polyprotein and synthetic peptide substrates of human immunodeficiency virus (HIV) origin with an efficiency that can approach that exhibited by HIV proteinase. EIAV proteinase, however, was not susceptible to inhibition by a wide variety of inhibitors HIV-1 proteinase, including those which have been licensed as anti-AIDS drugs. In this respect, EIAV proteinase behaves like an extreme case of a drug-resistant mutant of HIV-1 proteinase that has arisen under selective drug pressure. Only one potent inhibitor (HBY-793) of HIV-1 proteinase showed comparable efficiency against the EIAV enzyme; the compds. A-77003 and A-76889, which differ only in their stereochem. and which are otherwise structurally identical to HBY-793 from residues P2 to P2' [nomenclature of Schechter, I. & Berger, A. (1967) Biochem. Biophys. Res. Commun. 27, 157-162], were not effective inhibitors of EIAV proteinase. Mutant forms of EIAV proteinase (Thr30→Asp and Ile54→Gly) were generated and their ability to interact with substrates and inhibitors was characterized. HBY-793 inhibited [Gly54]proteinase as effectively as the wild-type proteinase but was tenfold less potent against [Asp30]proteinase. Data interpretations are presented, based on the structure solved for the complex between HBY-793 and EIAV [Gly54]proteinase [Gustchina A., Kervinen, J., Powell, D. J., Zdanov, A., Kay, J. & Wlodawer, A. (1996) Protein Sci. 5, 1453-1465].

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); BIOL (Biological study)
(substrate specificity, susceptibility to HIV proteinase inhibitors, ability to process HIV gag polyprotein, and mutagenesis of recombinant aspartic proteinase from equine infectious anemia virus)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



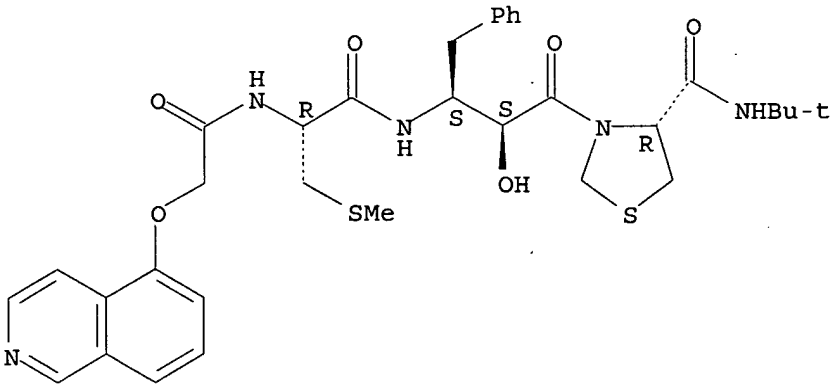
L83 ANSWER 49 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:689348 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 126:429
TITLE: Bound water molecules at the interface between the HIV-1 protease and a potent inhibitor, KNI-272, determined by NMR
AUTHOR(S): Wang, Yun-Xing; Freedberg, Daron I.; Wingfield, Paul T.; Stahl, Stephen J.; Kaufman, Joshua D.; Kiso, Yoshiaki; Bhat, T. Narayana; Erickson, John W.; Torchia, Dennis A.
CORPORATE SOURCE: Molecular Structural Biology Unit, National Institute of Dental Research, Bethesda, MD, 20892, USA
SOURCE: Journal of the American Chemical Society (*1996*), 118(49), 12287-12290
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KNI-272 is a peptidomimetic transition state analog inhibitor, having very high specificity and binding affinity for the HIV-1 protease. In order to understand the interactions that enhance drug binding to the protease, we recorded 2D water/NOESY and water/ROESY spectra to identify water mols. that bind tightly to the protease/KNI-272 complex. Well-ordered water mols. are observed at the protease/inhibitor interface in the crystal structure of the complex that have short interproton distances to the Ile50/150, Ala28/128, and Asp29/129 amide protons. The cross peaks between these protein protons and water protons, observed in water/NOESY and water/ROESY spectra, provide strong evidence that these water mols. are present in the solution structure of the complex. Anal. of measured NOE and ROE cross relaxation rates indicates that, in solution, these water mols. have long residence times, at least 1 ns and possibly greater than 7 ns. The presence of long-lived hydration water mols. at the protein/inhibitor interface suggests that interactions involving these water mols. contribute to the potency of the inhibitor. Hence, consideration of the potential role of hydration water mols. in stabilizing protein/inhibitor structures could contribute to improved drug design and to a better understanding of the mechanisms of drug resistance.

IT *147318-81-8*, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BPR (Biological process); BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); PROC (Process); USES (Uses)
(NMR study of hydration water mols. at interface between HIV-1 protease and inhibitor KNI-272 in relation to AIDS)

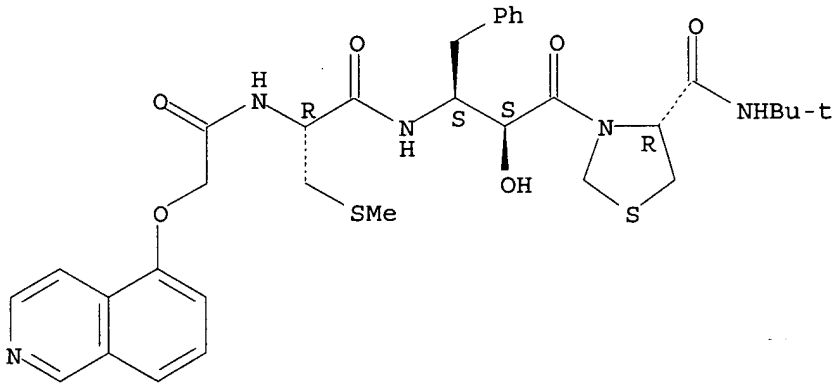
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT ***147318-81-8D***, KNI-272, complexes with HIV-1 protease
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative)
(NMR study of hydration water mols. at interface between HIV-1 protease and inhibitor KNI-272 in relation to AIDS)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



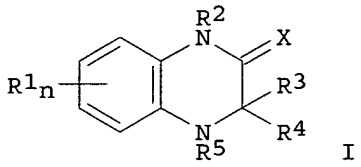
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L83 ANSWER 50 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:601709 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 125:238651
TITLE: Use of quinoxalines and protease inhibitors in a composition for the treatment of AIDS and/or HIV infections
INVENTOR(S): Paessens, Arnold; Blunck, Martin; Riess, Guenther; Kleim, Joerg-Peter; Roesner, Manfred
PATENT ASSIGNEE(S): Bayer A.-G., Germany
SOURCE: Eur. Pat. Appl., 24 pp.

CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 728481	A2	19960828	EP 1996-102129	19960214 <--
EP 728481	A3	19980708		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
DE 19506742	A1	19960829	DE 1995-19506742	19950227 <--
AU 9645615	A1	19960905	AU 1996-45615	19960220 <--
AU 710158	B2	19990916		
CA 2170222	AA	19960828	CA 1996-2170222	19960223 <--
FI 9600850	A	19960828	FI 1996-850	19960223 <--
JP 08245392	A2	19960924	JP 1996-60286	19960223 <--
IL 117247	A1	20001031	IL 1996-117247	19960223 <--
NO 9600775	A	19960828	NO 1996-775	19960226 <--
ZA 9601516	A	19960903	ZA 1996-1516	19960226 <--
BR 9600809	A	19971223	BR 1996-809	19960226 <--
CN 1141196	A	19970129	CN 1996-102709	19960227 <--

PRIORITY APPLN. INFO.: DE 1995-19506742 A 19950227 <--
OTHER SOURCE(S): MARPAT 125:238651
GI



I

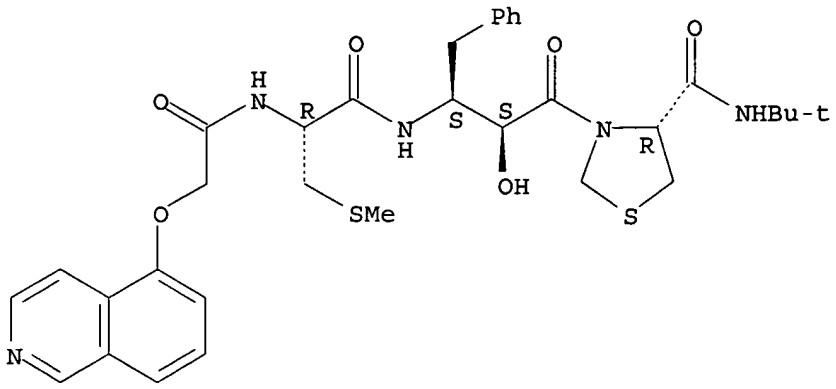
AB Combinations of a quinoxaline derivative [I; R1 = halo, OH, NO2, (substituted) amino, N3, CF3, CF3O, C1-8 alkyl, CN, (substituted) Ph, N-heterocyclyl, etc.; R2, R5 = H, OH, C1-6 alkoxy, aryloxy, C1-6 acyloxy, CN, (substituted) amino, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 alkynyl, (substituted) C3-8 cycloalk(en)yl, etc.; R3, R4 = H, (substituted) C1-8 alkyl, (substituted) C2-8 alkenyl, (substituted) C3-8 cycloalk(en)yl, (substituted)aryl, etc.; or R3R4 or R3R5 complete a (substituted) ring; X = O, S, Se, NR2; n = 0-4] and a peptidomimetic protease inhibitor are useful for treatment of HIV infections and AIDS. Thus, I [R1 = 6-MeO, R2 = R3 = H, R4 = (S)-MeSCH2, R5 = i-PrO2C, X = S] (0.7-6 nM) and saquinavir (6-50 nM) synergistically inhibited syncytium formation in HIV-infected human lymphocytes in vitro.

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(use of quinoxalines and protease inhibitors for treatment of AIDS and HIV infections)

RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-

[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 51 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:594448 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 125:292250
TITLE: A diarylsulfone non-nucleoside reverse transcriptase inhibitor with a unique sensitivity profile to drug-resistant virus isolates
AUTHOR(S): Buckheit, R. W., Jr.; Fliakas-Botlz, V.; Russell, J. D.; Snow, M.; Pallansch, L. A.; Yang, S. S.; Bader, J. P.; Khan, T. N.; Zanger, M.
CORPORATE SOURCE: Virology Res. Group, Southern Res. Inst.-Frederick Res. Center, Frederick, MD, 21701, USA
SOURCE: Antiviral Chemistry & Chemotherapy (*1996*), 7(5), 243-252
CODEN: ACCHEH; ISSN: 0956-3202
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Structure-activity relationship evaluations with a series of diarylsulfone non-nucleoside reverse transcriptase (RT) inhibitors indicated that the steric properties of the mol. and compound lipophilicity primarily contributed to the overall level of activity of the compds. against human immunodeficiency virus type 1 (HIV-1). The most active compds. in the diarylsulfone series had an orthonitro group and yielded anti-HIV activity at sub-micromolar concns. Compds. of the diarylsulfone class exhibited antiviral properties similar to other members of the pharmacol. class of HIV-1 specific nonnucleoside reverse transcriptase inhibitors, including activity in a wide variety of established and primary human cells, activity against a wide variety of laboratory and clin. virus isolates, and activity when challenged at high multiplicity of infection. Synergistic inhibition of HIV-1 was observed when the diarylsulfone NSC 667952 was used with the nucleoside analogs AZT, DDI, 3Tc and d4T, the protease inhibitor KNI 272 and the sulfoanted dye resobene; additive effects were observed when NSC 667952 was used with the nucleoside analog ddC and other non-nucleoside RT inhibitors. The diarylsulfones exhibited a unique sensitivity profile when evaluated against both virus isolates and purified reverse transcriptase containing non-nucleoside reverse transcriptase

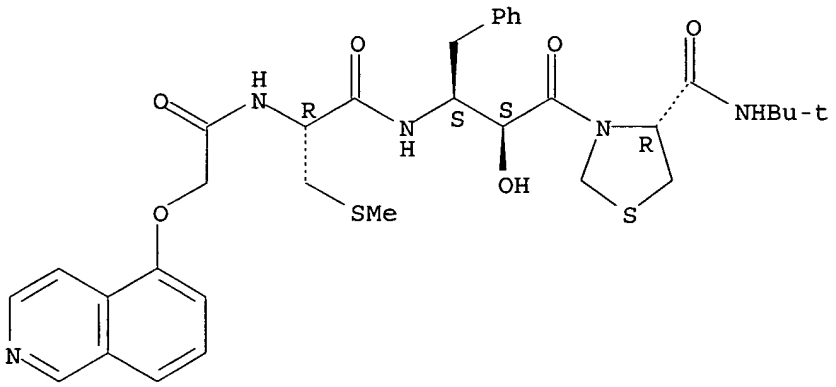
inhibitor resistance-engendering mutations. Unlike other members of the class of nonnucleoside compds., NSC 667952 remained active against virus isolates with the L100I amino acid change in the RT. The compound was, however, highly sensitive to Y181C, K103N and K101E amino acid changes in the RT. The diarylsulfone selected for resistant virus populations which possessed the Y181C amino acid change in the reverse transcriptase and which exhibited enhanced sensitivity to the nonnucleoside inhibitors calanolide A and costatolide.

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(anti-HIV-1 activity of diarylsulfone non-nucleoside reverse transcriptase inhibitor in relation to drug resistance and structure)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 52 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:321527 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 125:87115
TITLE: Design and synthesis of substrate-based peptidomimetic human immunodeficiency virus protease inhibitors containing the hydroxymethylcarbonyl isostere
AUTHOR(S): Kiso, Yoshiaki
CORPORATE SOURCE: Dep. Med. Chem., Kyoto Pharmaceutical Univ., Kyoto, 607, Japan
SOURCE: Biopolymers (***1996***), 40(2), 235-244
CODEN: BIPMAA; ISSN: 0006-3525
PUBLISHER: Wiley
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 27 refs. The human immunodeficiency virus (HIV) codes for an aspartic protease are known to be essential for retroviral maturation and replication. The HIV protease can recognize Phe-Pro and Tyr-Pro sequences as the virus-specific cleavage site. These features provided a basis for the rational design of selective HIV protease-targeted drugs for the treatment of acquired immunodeficiency syndrome (AIDS). We replaced

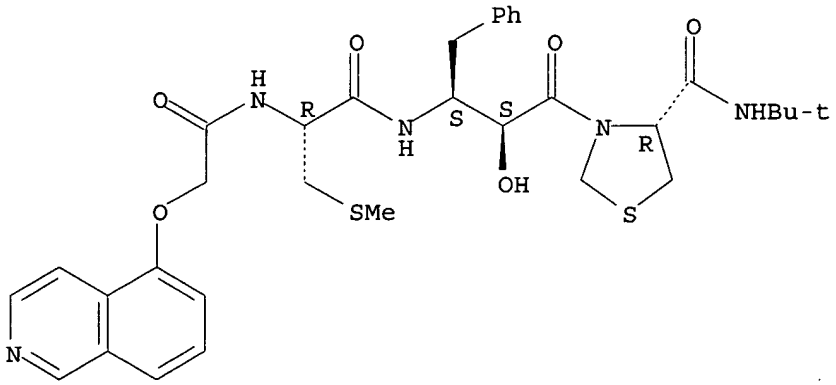
the two Cys residues by L-Ala to synthesize [Ala67,95]-HIV-1 protease by the solid phase method and then prepared [Tyr6,42,Nle36,46,(NHCH2COSCH2CO)51-52,Ala67,95]HIV-1 protease (NY-5 isolate) using the thioester chemical ligation method. Based on the substrate transition state, we designed and synthesized a novel class of HIV protease inhibitors containing an unnatural amino acid, (2S, 3S)-3-amino-2-hydroxy-4-phenylbutyric acid, named allophenylnorstatine (Apns) with a hydroxymethylcarbonyl (HMC) isostere. Among them, the conformationally constrained tripeptide kynostatin (KNI)-272 (iQoa-Mta-Apns-Thz-NHBut) was a highly selective and superpotent HIV protease inhibitor (Ki = 0.0055 nM). The X-ray crystallog. and mol. modeling studies showed that the HMC group in KNI-272 interacted excellently with the aspartic acid carboxyl groups of HIV protease active site in the essentially same hydrogen-bonding mode as the transition state. This result implies that the HMC isostere is an ideal transition-state mimic and contributes to the high activity of KNI-272.

IT ***147318-81-8P***, Kni-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design and synthesis of substrate-based peptidomimetic human immunodeficiency virus protease inhibitors containing the hydroxymethylcarbonyl isostere)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 53 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:313379 CAPLUS <<LOGINID::20060922>>

DOCUMENT NUMBER: 125:75406

TITLE: Assessment of a cytoprotection assay for the discovery and evaluation of anti-human immunodeficiency virus compounds utilizing a genetically-impaired virus

AUTHOR(S): Kiser, Rebecca; Makovsky, Susan; Terpening, Sara J.; Laing, Noel; Clanton, David J.

CORPORATE SOURCE: NCI-AIDS Drug Screening and Development Laboratory, SAIC-Frederick, NCI-FCRDC, Frederick, MD, 21702-1201, USA

SOURCE: Journal of Virological Methods (***1996***),

58(1,2), 99-109
CODEN: JVMEDH; ISSN: 0166-0934
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

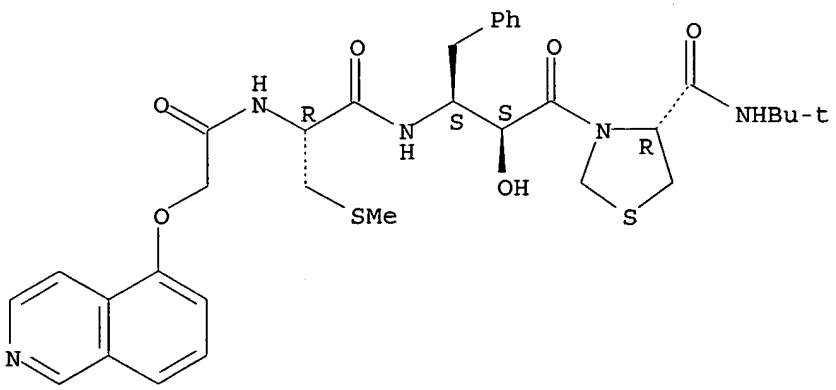
AB A biol. contained cytoprotection assay was developed to screen inhibitors of the human immunodeficiency virus without the need for high level containment or practices. The virus used has multiple point mutations that have destroyed its ability to produce both Rev and Tat, proteins essential for virus replication in vitro. The original cell line employed (CEM-SSTART) contains a genetic construct that allows for the continuous expression of both Rev and Tat, and a subclone (1A2) was developed that provides for maximum acute cytopathic effect. The National Cancer Institute's AIDS drug screening assay was used to test known drugs with both HIVIIIB virus in the T4 lymphocytic cell line CEM-SS and mutant virus in the 1A2 subclone. This cell-based assay uses the tetrazolium salt, XTT, as an indicator of cellular metabolism after the cells have been infected with virus. The results of extensive testing have shown that the assay using mutant virus is comparable to the current NCI AIDS drug screen. After 42 days in 1A2 or CEM-SS cell culture, the virus or the integrated genome did not revert to wild-type, and the virus produced in 1A2 cells was unable to replicate in PBMCs. Mutant viral stocks were devoid of wild-type virus as determined by a PCR assay that would have found 60-600 copies of mutant RNA. These materials, which are now available to the scientific community (NIH AIDS Research and Reference Reagent Program), should be useful tools to screen and test compds. for potential inhibition of HIV in labs. not equipped to maintain and use wild-type infectious virus.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(assessment of cytoprotection assay for discovery and evaluation of anti-human immunodeficiency virus compds. utilizing a genetically-impaired virus)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



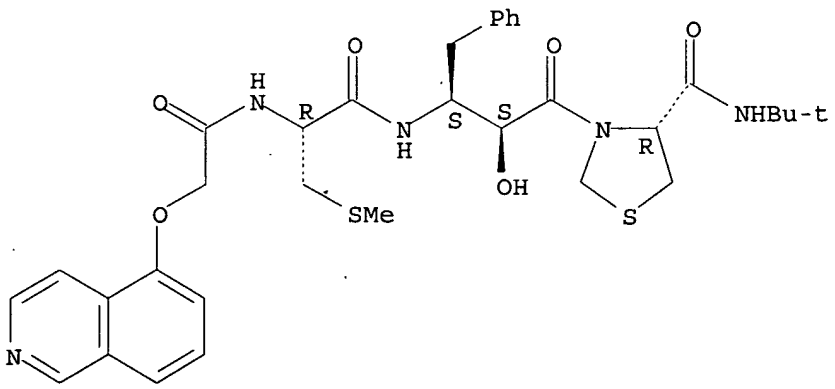
L83 ANSWER 54 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:189956 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 124:306583
TITLE: FR901724, a novel anti-human immunodeficiency virus (HIV) peptide produced by Streptomyces, shows synergistic antiviral activities with HIV protease inhibitor and 2',3'-dideoxynucleosides
AUTHOR(S): Nakashima, Hideki; Ichiyama, Kohji; Inazawa, Kazuhiko; Ito, Masahiko; Hayashi, Hideya; Nishihara, Yutaka; Tsujii, Eisaku; Kino, Toru
CORPORATE SOURCE: Dep. Microbiology, Yamanashi Medical Univ., Yamanashi, 409-38, Japan
SOURCE: Biological & Pharmaceutical Bulletin (*1996*), 19(3), 405-12
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel tricyclic 21-amino-acid peptide, FR901724, was isolated from the cultured broth of Streptomyces sp. Number 73264. This peptide appears to possess potent anti-human immunodeficiency virus (HIV) activity in vitro and might represent a lead to a new class of anti-HIV agents; it quantifies as an HIV-cell fusion inhibitor because of its weak inhibition ov virus-cell binding and strong inhibition of syncytium formation. From the time-of-addition expts., the mode of action of FR901724 was found to definitely differ from that KNI-272, a peptide mimetic allophenylmorstatine-derivative HIV protease inhibitor. FR 901724 appears to interact with a stage of the virus replicative cycle that may well correspond to virus-cell fusion. We also found that FR901724 was synergistic or had a strong tendency toward synergism when combined with other antiviral drugs, such as KNI-272, AZT, ddI and dextran sulfate.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(FR901724, a novel anti-human immunodeficiency virus (HIV) peptide produced by Streptomyces, shows synergistic antiviral activities with HIV protease inhibitor and 2',3'-dideoxynucleosides)

RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



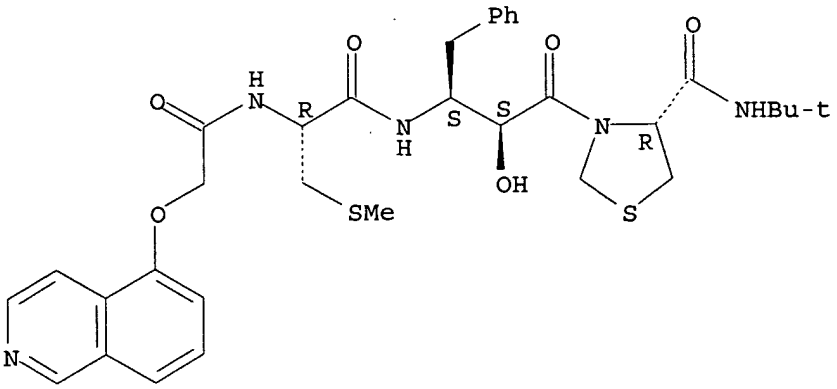
L83 ANSWER 55 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:182128 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 124:278084
TITLE: The bioavailability of oral dosage forms of a new HIV-1 protease inhibitor, KNI-272, in beagle dogs
AUTHOR(S): Kiriyama, A.; Sugahara, M.; Yoshikawa, Y.; Kiso, Y.; Takada, K.
CORPORATE SOURCE: Dep. Pharmaceutics and Pharmacokinetics, Kyoto Pharmaceutical Univ., Kyoto, 607, Japan
SOURCE: Biopharmaceutics & Drug Disposition (*1996*), 17(2), 125-34
CODEN: BDDID8; ISSN: 0142-2782
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bioavailability (BA) of a tripeptide protease inhibitor, KNI-272, which has a strong pharmacol. potential for treating human immunodeficiency virus type 1 (HIV-1), has been studied in beagle dogs by administering several oral dosage forms. The tested dosage forms were form 1, plain gelatin capsules; forms 2 and 3, gelatin capsules of which the inner and outer surfaces were coated with 7G ethylcellulose (EC, 30 μm thickness) and an enteric coating material, hydroxypropyl methylcellulose phthalate (HP-55), resp.; and form 4, gelatin capsules of which the inner surface is coated with 10G EC (60 μm thickness). The difference between forms 2 and 3 was the amount of citric acid contained in the capsule, namely 100 mg in form 2 and 200 mg in form 3. One hundred milligrams of KNI-272 was placed in each capsule after being dissolved with propylene glycol (PG). These capsules were used to deliver KNI-272 to the stomach for form 1, to the upper part of the small intestine for forms 2 and 3, and to the middle part of the small intestine for form 4. As a reference, 50.0 mg of KNI-272 was administered to the same dogs by i.v. (IV) infusion for 15 min. By measuring the plasma drug levels with the HPLC method, BAs were estimated for each test dosage form. Form 1 showed the highest BA of 26.2%, though the other capsules showed BAs of approx. 10%, namely 6.6% for form 2, 10.3% for form 3 and 14.2% for form 4. Therefore, as the site where KNI-272 is released from the capsule becomes higher, the BA increases. In addition, as the amount of citric acid contained in a capsule increases, the BA value tends to increase. These results suggest that KNI-272 is stable and not extensively hydrolyzed in the gut after oral administration, that the dissoln. process into GI fluids is important for the BA of KNI-272, and that the most appropriate absorption site of KNI-272 in dogs is the duodenum. The potential of this new tripeptide compound as an orally active anti-AIDS drug has been confirmed.

IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BPR (Biological process); BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); PROC (Process); USES (Uses)
(bioavailability of oral dosage forms of a new HIV-1 protease inhibitor, KNI-272, in beagle dogs)

RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

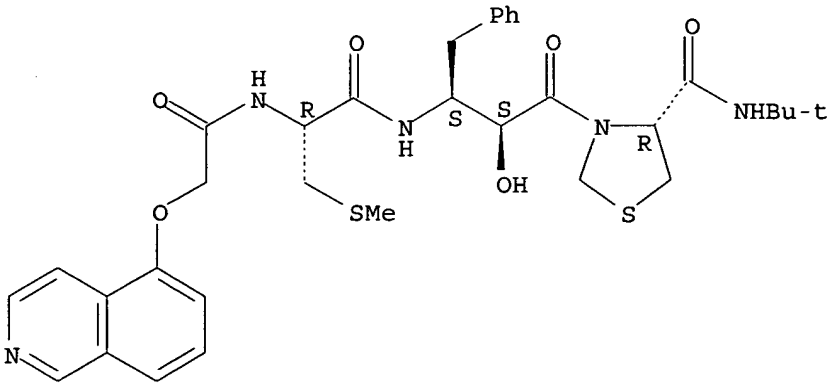


L83 ANSWER 56 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:936335 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 124:44750
TITLE: Design and synthesis of HIV protease inhibitors containing allophenylnorstatine as a transition-state mimic
AUTHOR(S): Kiso, Yoshiaki
CORPORATE SOURCE: Department Medicinal Chemistry, Kyoto Pharmaceutical University, Kyoto, 607, Japan
SOURCE: Advances in Experimental Medicine and Biology (***1995***), 362(Aspartic Proteinases), 413-23
CODEN: AEMBAP; ISSN: 0065-2598
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Based on the transition state of the HIV protease, a novel class of peptidyl HIV protease inhibitors containing allophenylnorstatine was designed and synthesized. The critical OH group as a transition-state mimic interacts with the aspartate CO2H groups of the active site of the HIV protease; the stereochem. of the OH group is significant for producing inhibition. One compound, KNI-272, warrants further studies for clin. use as an oral anti-HIV drug because of its ease of synthesis, specific inhibition of HIV protease, potent antiviral properties, and favorable cytotoxicity profile.

IT ***147318-81-8P***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(peptide-type HIV protease inhibitors containing allophenylnorstatine)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

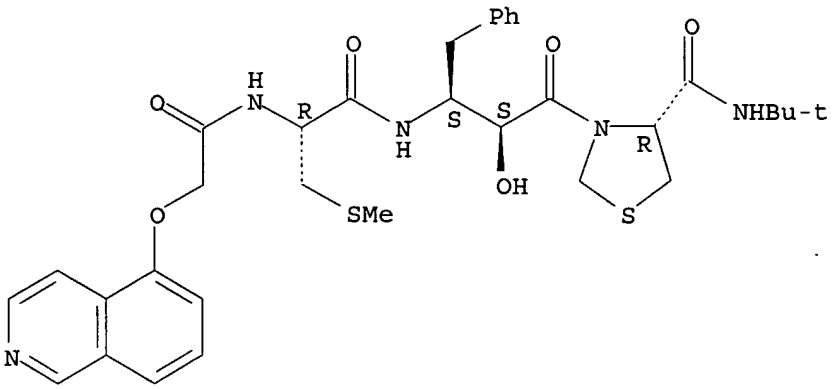


L83 ANSWER 57 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:790958 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 123:275271
TITLE: In vitro anti-HIV-1 activity of HIV protease inhibitor KNI-272 in resting and activated cells: implications for its combined use with AZT or ddI
AUTHOR(S): Chokekijchai, Sudhichai; Shirasaka, Takuma; Weinstein, John N.; Mitsuya, Hiroaki
CORPORATE SOURCE: The Experimental Retrovirology Section, Medicine Branch, National Cancer Institute, Bldg 10, Rm 5A11, Bethesda, MD, 20892, USA
SOURCE: Antiviral Research (*1995*), 28(1), 25-38
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KNI-272, a conformationally constrained human immunodeficiency virus (HIV) protease inhibitor containing a P1 allophenylnorstatine (Apns) ((2S,3S)-3-amino-2-hydroxy-4-phenylbutyric acid), has been shown to be a selective and potent inhibitor of the replication of a wide spectrum of HIV strains in vitro. When KNI-272 was tested in combination with 3'-azido-2',3'-dideoxythymidine (AZT) or 2',3'-dideoxyinosine (ddI) against a primary HIV-1 isolate in phytohemagglutinin-activated peripheral blood mononuclear cells (PHA-PBM), its activity was identified to be additive, but not synergistic or antagonistic, as analyzed with the COMBO program package. When tested alone for anti-HIV-1 activity in resting PBM (R-PBM) and PHA-PBM, KNI-272 was found to be comparably potent against the virus in both target cell populations, whereas AZT was more potent in PHA-PBM than in R-PBM and ddI was more potent in R-PBM. These data suggest a potential clin. application of KNI-272 and its analogs.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(anti-HIV-1 activity of HIV protease inhibitor KNI-272 in resting and activated cells: implications for its combined use with AZT or ddI)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 58 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:688810 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 123:163981
TITLE: Structure of HIV-1 protease with KNI-272, a tight-binding transition-state analog containing allophenylnorstatine
AUTHOR(S): Baldwin, Eric T.; Bhat, T. Narayana; Gulnik, Sergel; Liu, Beishan; Topol, Igor A.; Kiso, Yoshiaki; Mimoto, Tsutomu; Mitsuya, Hiroaki; Erickson, John W.
CORPORATE SOURCE: Frederick Biomedical Supercomputing Center, SAIC-Frederick, NCI-Frederick Cancer Research and Development Center, Frederick, MD, 21702, USA
SOURCE: Structure (London) (*1995*), 3(6), 581-90
CODEN: STRUE6; ISSN: 0969-2126
PUBLISHER: Current Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HIV-1 protease (HIV PR), an aspartic protease, cleaves Phe-Pro bonds in the Gag and Gag-Pol viral polyproteins. Substrate-based peptide mimics constitute a major class of inhibitors of HIV PR presently being developed for AIDS treatment. One such compound, KNI-272, which incorporates allophenylnorstatine (Apns)-thioproline (Thp) in place of Phe-Pro, has potent antiviral activity and is undergoing clin. trials. The structure of the enzyme-inhibitor complex should lead to an understanding of the structural basis for its tight binding properties and provide a framework for interpreting the emerging resistance to this drug. The three-dimensional crystal structure of KNI-272 bound to HIV PR has been determined to 2.0 Å resolution and used to analyze structure-activity data and drug resistance for the Arg8→Gln and Ile84→Val mutations in HIV PR. The conformationally constrained Apns-Thp linkage is favorably recognized in its low energy trans conformation, which results in a sym. mode of binding to the active-site aspartic acids and also explains the unusual preference of HIV PR for the S, or syn, hydroxyl group of the Apns residue. The inhibitor recognizes the enzyme via hydrogen bonds to three bridging water mols., including one that is coordinated directly to the catalytic Asp125 residue. The structure of the HIV PR/KNI-272 complex illustrates the importance of limiting the conformational degrees of freedom and of using protein-bound water mols. for binding potent inhibitors. The binding mode of HIV PR inhibitors can be predicted from

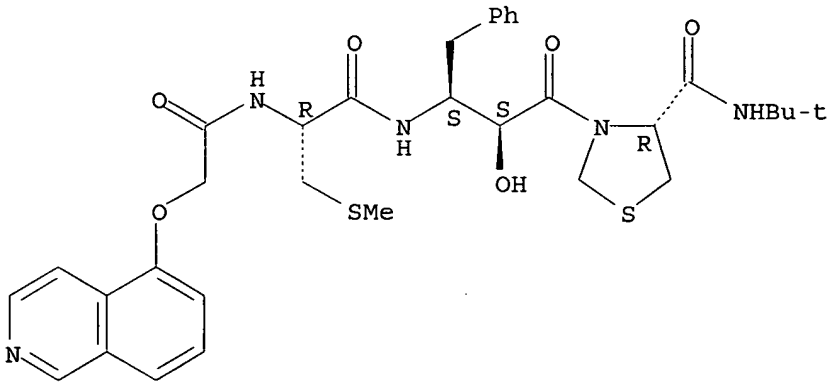
the stereochem. relation between adjacent hydroxyl-bearing and side chain bearing carbon atoms of the P1 substituent. The structure also provides a framework for designing analogs targeted to drug-resistant mutant enzymes.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structure of HIV-1 protease with KNI-272 - a tight-binding transition-state analog containing allophenylnorstatine)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 59 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:683314 CAPLUS <<LOGINID::20060922>>

DOCUMENT NUMBER: 123:102100

TITLE: Kinetic Characterization and Cross-Resistance Patterns Of HIV-1 Protease Mutants Selected under Drug Pressure

AUTHOR(S): Gulnik, Sergei V.; Suvorov, Leonid I.; Liu, Beishan; Yu, Betty; Anderson, Barry; Mitsuya, Hiroaki; Erickson, John W.

CORPORATE SOURCE: Frederick Cancer Research and Development Center, National Cancer Institute, Frederick, MD, 21702-1201, USA

SOURCE: Biochemistry (***1995***), 34(29), 9282-7
CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Eleven different recombinant, drug-resistant HIV-1 protease (HIV PR) mutants-R8Q, V32I, M46I, V82A, V82F, V82I, I84V, V32I/I84V, M46I/V82F, M46I/I84V, and V321/K45I/F53L/A71V/I84V/L89M-were generated on the basis of results of in vitro selection expts. using the inhibitors A-77003, A-84538, and KNI-272. Kinetic parameters of mutant and wild-type (WT) enzymes were measured along with inhibition consts. (Ki) toward the inhibitors A-77003, A-84538, KNI-272, L-735,524, and Ro31-8959. The catalytic efficiency, kcat/Km, for the mutants decreased relative to WT by a factor of 1.2-15 and was mainly due to the elevation of Km. The effects

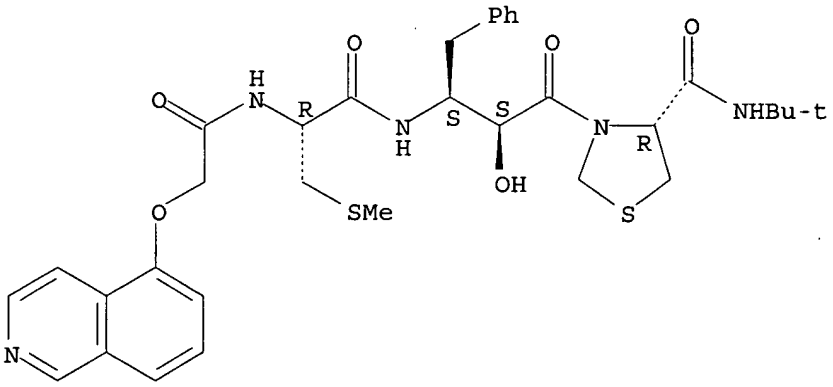
of specific mutations on Ki values were unique with respect to both inhibitor and mutant enzyme. A new property, termed vitality, defined as the ratio (Kikcat/Km)mutant/(Kikcat/Km)WT was introduced to compare the selective advantage of different mutants to an inhibitor. High vitality values were generally observed with mutations that emerged during in vitro selection studies. The kinetic model along with the panel of mutants described here should be useful for evaluating and predicting patterns of resistance for HIV PR inhibitors and may aid in the selection of inhibitor combinations to combat drug resistance.

IT ***147318-81-8***, KNI-272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(kinetic characterization and cross-resistance patterns of HIV-1 protease mutants selected under drug pressure)

RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 60 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:339426 CAPLUS <<LOGINID::20060922>>

DOCUMENT NUMBER: 122:133859

TITLE: preparation of peptides derivatives as intermediates for HIV protease inhibitors

INVENTOR(S): Maeda, Sadayuki; Moriwaki, Hiroki; Mitsumoto, Tsutomu; Kisanuki, Junji; Kato, Ryohei; Maeda, Hiroshi; Takahashi, Osamu; Kiso, Yoshiaki

PATENT ASSIGNEE(S): Japan Enajii Kk, Japan; Hamari Yakuhin Kogyo Kk

SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF

DOCUMENT TYPE: Patent

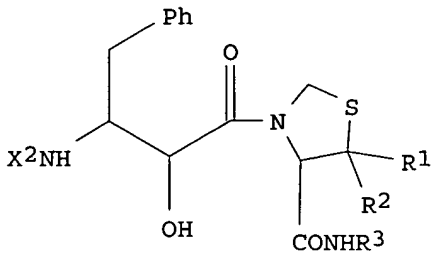
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

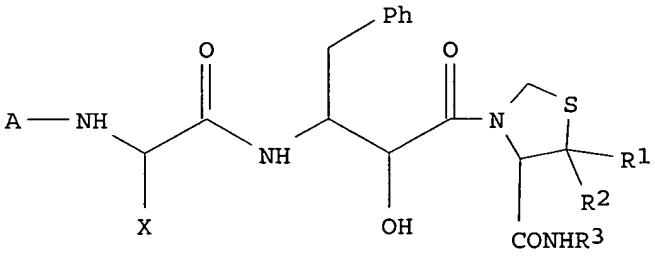
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06220031	A2	19940809	JP 1993-28546	19930125 <--

PRIORITY APPLN. INFO.: JP 1993-28546 19930125 <--
OTHER SOURCE(S): CASREACT 122:133859; MARPAT 122:133859
GI



I



II

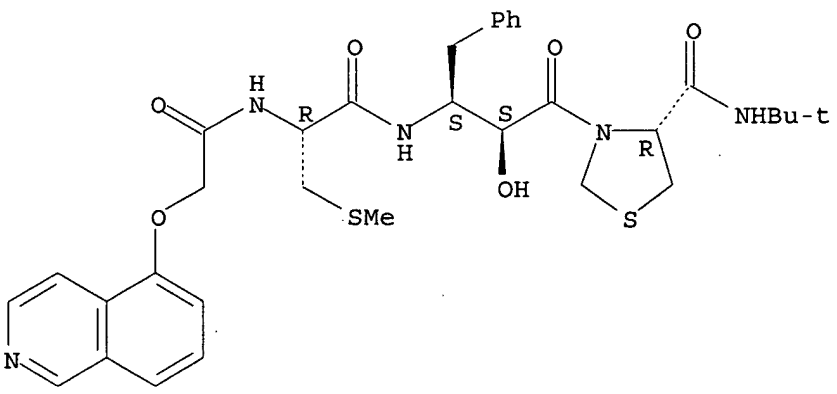
AB 1,3-Thiazolidine-4-carboxamides [I; R1, R2 = alkyl, H; R3 = alkyl; X2 = H2N-CHX-CO-] are reacted with A-NH-CHX-CO2H [A = amino protecting group] and (PhO)2P(O)B [B = azido, (un)substituted] to give the peptide derivs. II, useful as intermediates for HIV protease inhibitors. Thus, H-AHPBA-Thz-NH-tBu [AHPBA = 3-amino-2-hydroxy-4-phenylbutanoic acid residue; Thz = thiazolidine-4-carboxylic acid residue] (preparation given) was treated with BOC-Mta-OH [Mta = methylthioalanine residue] in DMF containing diphenylphosphoryl azide (DPPA) and Et3N at ≤8° overnight to give, after deprotection, H-Mta-AHPBA-Thz-tBu, which was reacted with Qoa-OH [Qoa = 5-isoquinolinyloxyacetic acid residue] in DMF containing DPPA and Et3N at 0° for 1 h to give Qoa-Mta-AHPBA-Thz-tBu.

IT ***147318-81-8P***
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); SPN (Synthetic preparation); ***THU (Therapeutic use)***; BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides derivs. as intermediates for HIV protease inhibitors)

RN 147318-81-8 CAPLUS

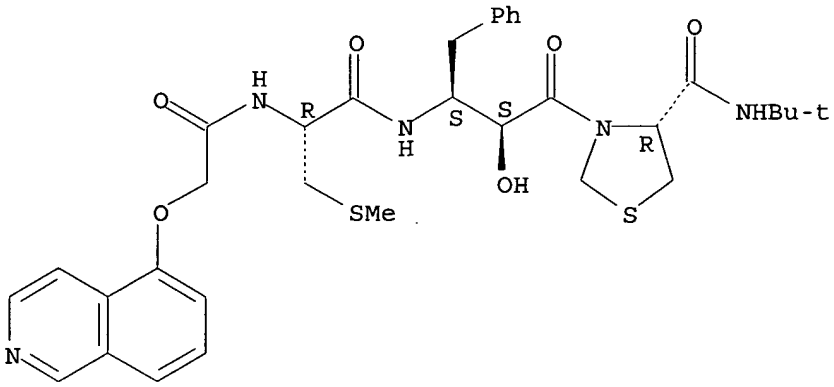
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

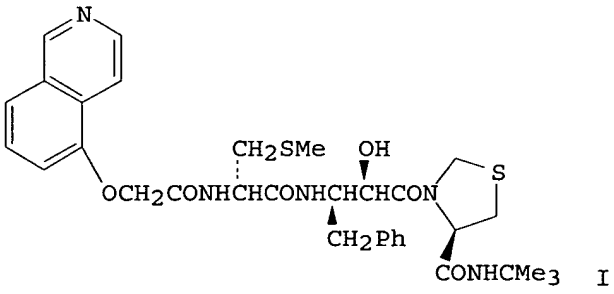


L83 ANSWER 61 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:69149 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 123:315
TITLE: The promising anti-HIV agent kynostatin (KNI)-272: a highly selective and super-active HIV protease inhibitor containing allophenylnorstatine
AUTHOR(S): Kiso, Y.; Mimoto, T.; Imai, J.; Kisanuki, S.; Enomoto, H.; Hattori, N.; Takada, K.; Akaji, K.; Kageyama, S.; Mitsuya, H.
CORPORATE SOURCE: Department of Medicinal Chemistry, Kyoto Pharmaceutical University, Kyoto, 607, Japan
SOURCE: Pept.: Chem., Struct. Biol., Proc. Am. Pept. Symp., 13th (*1994*), Meeting Date 1993, 619-21.
Editor(s): Hodges, Robert S.; Smith, John A. ESCOM: Leiden, Neth.
CODEN: 60LXAW
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Structure-activity studies on the penetration across the cell membrane and the behavior in vivo suggest that kynostatin-272 is a promising anti-HIV agent.
IT ***147318-81-8***
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(kynostatin-272 as anti-HIV agent)
RN 147318-81-8 CAPLUS
CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L83 ANSWER 62 OF 62 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:94734 CAPLUS <<LOGINID::20060922>>
DOCUMENT NUMBER: 120:94734
TITLE: Design and activity of protease active site-targeted anti-HIV agents containing allophenylnorstatin
AUTHOR(S): Mimoto, Tsutomu; Kisanuki, Sumitsugu; Imai, Junya; Enomoto, Hiroshi; Hattori, Naoko; Kageyama, Seiji; Mitsuya, Hiroaki; Akaji, Kenichi; Kiso, Yoshiaki
CORPORATE SOURCE: Dep. Med. Chem., Kyoto Pharm. Univ., Kyoto, 607, Japan
SOURCE: Pept. Chem. 1992, Proc. Jpn. Symp., 2nd ***(1993)***, ***Meeting Date 1992, 544-6. Editor(s): Yanaihara, Noboru. ESCOM: Leiden, Neth.***
CODEN: 59NTAC
DOCUMENT TYPE: ***Conference***
LANGUAGE: ***English***
GI



AB The antiviral activities of allophenylnorstatin-containing HIV protease inhibitors are discussed. KNI-272 (I) showed highly potent antiviral activity and low cytotoxicity.
IT ***147318-81-8***, KNI 272
RL: ***BAC (Biological activity or effector, except adverse)***; BSU (Biological study, unclassified); ***THU (Therapeutic use)***; BIOL (Biological study); USES (Uses)
(virucidal activity of, as HIV-1 protease inhibitor)
RN 147318-81-8 CAPLUS

CN 4-Thiazolidinecarboxamide, N-(1,1-dimethylethyl)-3-[(2S,3S)-2-hydroxy-3-[[(2R)-2-[[(5-isoquinolinyloxy)acetyl]amino]-3-(methylthio)-1-oxopropyl]amino]-1-oxo-4-phenylbutyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.